ICCB 2022

IX International Conference on Computational Bioengineering

11 - 13 April 2022

Instituto Superior Técnico | Lisbon | Portugal

BOOK OF ABSTRACTS

PROGRAM INCLUDED

Edited by:

Paulo R. Fernandes; João Folgado; Carlos Quental; André Castro

TÉCNICO LISBOA

idmec IST engenharia mecânica

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Title:

BOOK OF ABSTRACTS
IX International Conference on Computational Bioengineering

Edited by:

Paulo R. Fernandes, IDMEC, *Instituto Superior Técnico, Universidade de Lisboa, Portugal*

João Folgado, IDMEC, *Instituto Superior Técnico, Universidade de Lisboa, Portugal*

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First edition, **April 2022**

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Welcome Message

On behalf of the Organizing Committee, we are honored to welcome you to The Ninth International Conference on Computational Bioengineering (ICCB2022), hosted at Instituto Superior Técnico (IST), Universidade de Lisboa, Portugal, between April 11th and 13th, 2022. The ICCB conference series started in 2003 in Zaragoza, launched by Miguel Cerrolaza, Manuel Doblare, and Helder Rodrigues, and since then it has been organized every two years. Since 2003, renowned Researchers in the field have joined the steering committee and have taken the conference forward, making it a relevant forum to share, promote, and stimulate emerging interdisciplinary works on computational bioengineering. When the steering committee trusted us the organization of this edition, we received the decision with satisfaction and enthusiasm. It is great to have the opportunity to host a big event in Lisbon again, and to receive this research community in our house. However, a pandemic our generation had never seen changed all social rules, leading to a global lockdown. The first consequence was postponing this conference to 2022. As the pandemic evolved, and despite all other conferences moving to different formats, we remained hopeful that the situation would improve and would allow a face-to-face event. We invited a group of recognized keynote speakers, we promoted the organization of special sessions in very interesting topics and, finally, we are here in Lisbon all together for another ICCB. Even though its number of participants is lower than in previous editions, its high scientific standards were maintained, and we can once again have a face-to-face sharing of knowledge and discussion of advanced topics on computational bioengineering. So, our words are for all of you that participate in this conference. Notwithstanding the difficulties mentioned above, and now facing a war in Europe, you came to Lisbon to share your research. Thank you very much for your participation and contribution to the conference. Finally, we have to mention the conference's social program, which was defined to provide the participants a pleasant stay in Lisbon. This is the capital of Portugal, a historic city facing the Atlantic Ocean that has been a point of cultural interchange and encounter for many centuries. Lisbon has been welcoming visitors from all over the world, being recognized as one of the most beautiful places to visit. It is a safe and pleasant city where delegates and their companions will feel at ease and very well received. To conclude, we wish you a very productive and pleasant conference as well as an enjoyable stay in Portugal.

Lisboa, April 2022
Paulo R. Fernandes and João Folgado

Contents

Conference Organization

Executive Committee

Paulo R. Fernandes (Portugal)
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Carlos Quental (Portugal)
André Castro (Portugal)

Steering Committee

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Renato Natal Jorge (Portugal)
Rui Ruben (Portugal)
Sara Checa (Germany)
Scott Hollister (USA)
Stephane Avril (France)
Taiji Adachi (Japan)
William Taylor (Switzerland)

Conference Information

Endorsed by

IDMEC - Instituto de Engenharia Mecânica
Técnico Lisboa - Instituto Superior Técnico
Caixa Geral de Depósitos

Conference Venue

The **IX International Conference on Computational Bioengineering** takes place in Instituto Superior Tecnico (IST) Congress Center, situated at the Civil Engineering Building (Pavilhão de Civil) with the address:

Congress Center
(Civil Engineering Building)
Instituto Superior Técnico
Av. Rovisco Pais 1
1049-001 Lisboa

Secretariat Open Hours

- Monday, April 11, 08:00 -17:00
- Tuesday, April 12, 08:45 -15:30
- Wednesday, April 13, 08:45 -15:30

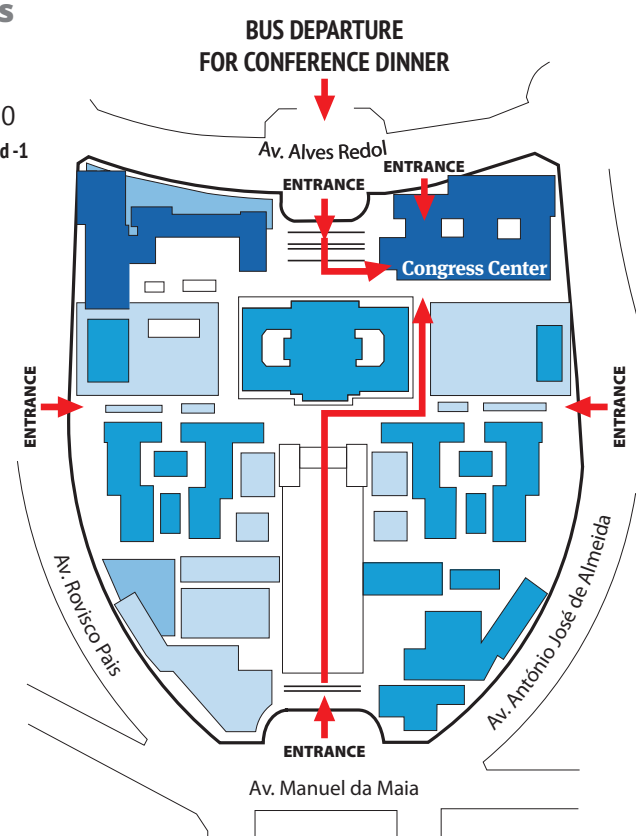
Congress Center (Civil Engineering Building) Ground -1

Coffee-Breaks

The coffee-breaks will take place in the hall -2 (2nd Basement) of the conference center (see map of the conference center) and will be open to all participants. Kindly wear your Conference Badge.

Lunches

Lunch will take place in the hall -2 (2nd Basement) of the conference center (please see map) and will be open to all participants. Kindly wear your conference badge. A few self-service choices will be offered for lunch, including a daily vegetarian option.



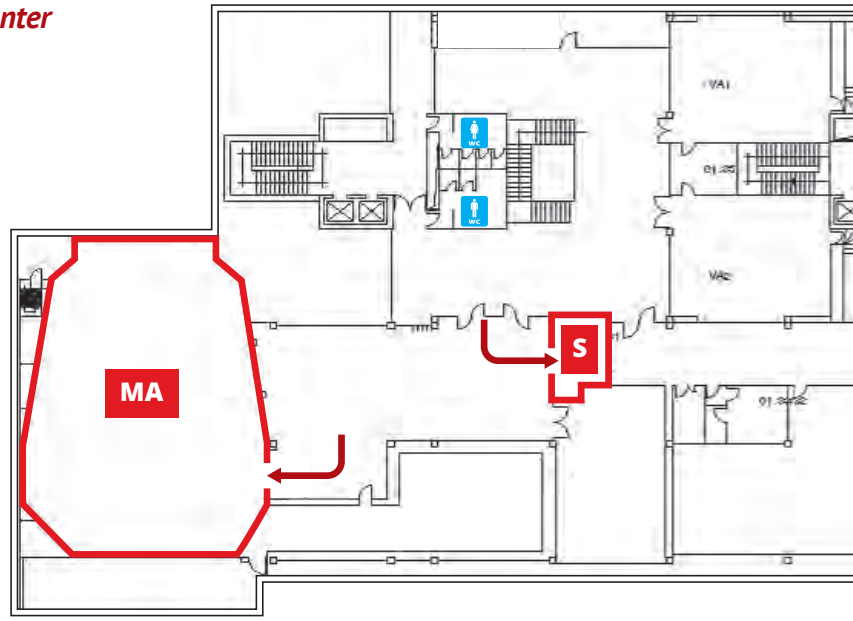
Plant

Instituto Superior Técnico

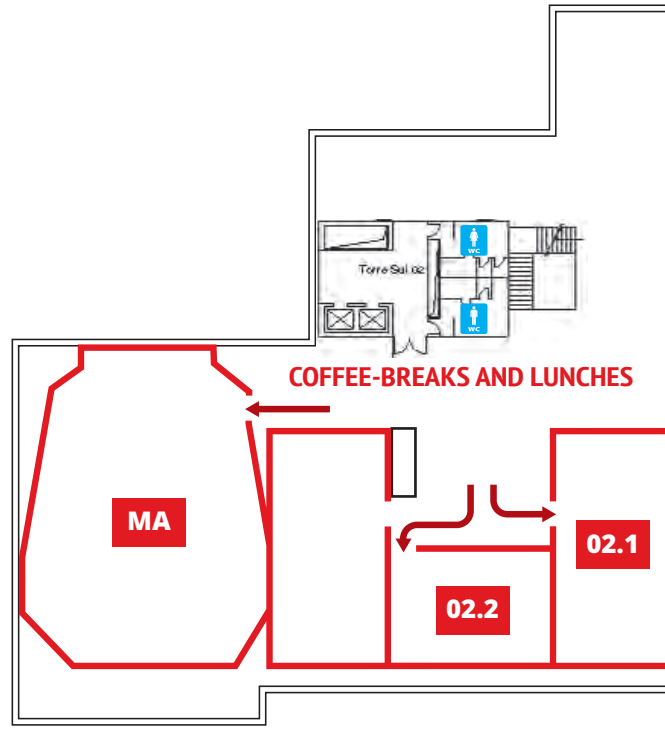
Conference Information

Congress Center Floor Plans

Congress Center
Floor -1
(1st Basement)



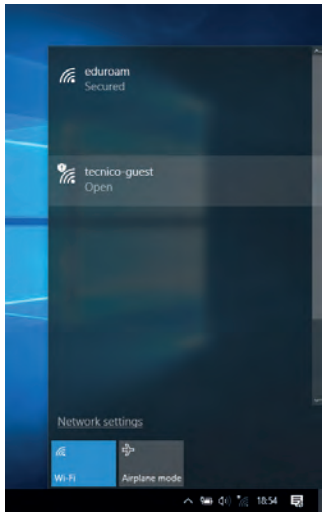
Congress Center
Floor -2
(2nd Basement)

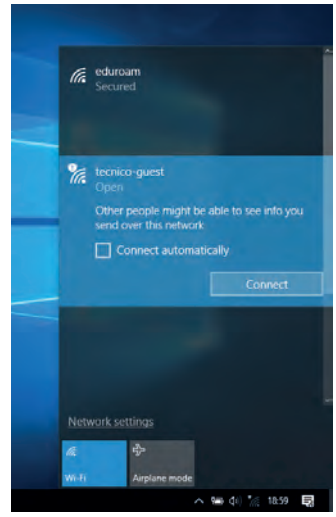


MA - Main Auditorium
S - Secretariat
02.1 - Session Room
02.2 - Session Room

Conference Information

Wireless Internet Access





Step 1: Browse available wireless networks and select **"tecnico-guest"**

Step 2: Open your web browser and access the website **"wifi.ist.utl.pt"** (most of the computers will do it automatically)

Step 3: Click on the (blue) button **"Ligar"**

Step 4: Enter the following credentials:

Account name: **ICCB2022**
Password: **fzKT8g**

Instructions for Presenters

- Each Oral presentation will take 15 minutes including discussion.
- The files required for the presentation (PowerPoint or PDF) should be uploaded, and tested to ensure compatibility, during the coffee or lunch breaks before the beginning of the session.
- The lecture rooms contain a Windows PC, with Office and Acrobat PDF Reader, connected to a data projector. The use of personal computers is not recommended.
- Technical support will be provided on-site by the ICCB2022 staff to ensure a smooth delivery of all presentations.

Social Program

Welcome Reception

Monday, 11st April 17h

The Welcome reception will take place at conference site.

Sailing Tour on the Tagus River

Tuesday, 12th April 16h

The bus will depart from **IST** (Rua Alves Redol) at 16H. Please be there 10 minutes prior to departure and do not forget to bring your tour/dinner voucher.

*We will depart to Doca do Espanhol, where we will board the **Ópera Boat**. We will be able to admire the beautiful sunset while sailing in the calm waters of the river. Enjoy magnificent views of the city's most famous monuments plus UNESCO World Heritage sites Belém Tower and Jerónimos Monastery.*

Conference Dinner

Tuesday, 12th April

The conference dinner will be on board of the ***Ópera Boat.*** The Tour/Dinner will end at 21 h.
The bus will bring you back to IST.

The estuary of the Tagus (19 km long) is one of Europe's finest harbors.
One of the longest suspension bridges in Europe, the Ponte 25 de Abril, spans this estuary.
Tagus' waters are usually calm and navigable for circa 130 km upstream.
The train along "Linha de Cascais" (departing from Cais do Sodré) follows Tagus' course until its meeting with the Atlantic Ocean.

General Tourist Information

Getting to Lisbon by air

Direct flights from most of European cities, North or South America and Africa land at the Portela Airport, terminal 1. A taxi ride from the airport to IST is about 4-5 km that takes 10-15 min, depending on traffic, and should cost around 8€. To downtown the taxi ride is about 7 km and should cost around 10€. 1.60€ is charged for the transportation of luggage or animals. A sure option is the "Taxi Voucher" a prepaid taxi service starting at 16.40€, on sale at the "Information Desk" in the arrival terminal. Lisbon Airport has its own Metro Station, Aeroporto - red line (see map of Lisbon with subway lines). Other options are the AeroBus and the Aeroshutle (3.5€).

Getting to Lisbon by car

Drivers can use highway A1 when coming from the North, highway A2, through the 25 de Abril bridge, when coming from the South, and highway A12, through Vasco da Gama bridge, when coming from the Northeast.

Getting to Lisbon by train

The St. Apolónia station is the terminal for trains arriving from the North of Portugal. Another option is to use the train station Oriente. From the South of Portugal an option is to use the train station Oriente. Connections to the metro lines exist at both stations (St. Apolónia - blue line, Oriente - red line).

Moving around

Taxi:

Lisbon is served by an extensive network of public transportation that can take you anywhere in the city and to its surroundings. Taxis (black and green or beige) are cheap when comparing to most of the European countries. They can be called by phone, picked-up on taxi plazas or stopped on the street. The fare on the taxi meter should start at 3.25€ (daytime pick-up) or 3.90€ (nighttime). Outside the city limits, city fares are charged per kilometer. 1.60€ is charged for the transportation of luggage or animals. Before taking a taxi, inquire about the fare.

Metro:

The Lisbon Metro is a very comfortable and an easy way to reach most of the city, from 6:30 to 1:00. The Metro lines reach most of the city being the Metro stations close to IST:

- Alameda (red and green line)
- Saldanha (red and yellow line)

Bus

The bus routes cover all Lisbon and extend to its outskirts. The tickets can be pre-paid, at the counters of Carris, the surface transportation operator for Lisbon, or bought aboard the bus, electric cars or funiculars.

For IST hop off on one of the following bus stops:
Av. Manuel da Maia
Av. Rovisco Pais
Arco do Cego

Metro and Bus Fares:

Reusable card – 0,50 €
METRO/CARRIS – 1,50 €
CARRIS Bus – 2,00 € (on board fare)
Tram – 3,00 € (on board fare)

Trains

Suburban trains to Estoril and Cascais depart from the Cais do Sodré train station, to the south of the river cities from Roma-Areeiro (Entrecampos) while to Sintra the trains depart from Rossio train station or Oriente (Entrecampos). The ride to Cascais or to Sintra should take about 35-45 min, each way. The train ride to south of the river is a highlight as the train will cross the 25 de Abril bridge with magnificent views of Lisbon.

For IST the nearby train stations are:
Roma-Areeiro
Entrecampos

Other general information

- **National emergency number:** 112
- **Time zone:** GMT +1 summer time
- **Electricity:** 220V, 50 Hz with standard European power sockets
- **Temperature:** Average high 19ºC, Average low 13ºC
- **Currency:** Euro (€)
- **Banks:** working hours are 8:30 – 15:00 (Monday-Friday)
- **Pharmacies:** 9:00 – 19:00
- **Shops:** 9:00 – 19:00
- **Shopping Malls:** 10:00 – 23:00

Main Museums in Lisbon:

- **Centro de Arte Moderna** *(Modern Art Museum)*
- **Museu do Oriente** *(Oriente Museum)*
- **Museu Calouste Gulbenkian** *(Calouste Gulbenkian Museum)*
- **Museu dos Coches** *(Coach Museum)*
- **Museu Nacional de Arte Antiga** *(National Museum for Ancient Art)*
- **Colecção Berardo** *(The Berardo Collection)*
- **Museu do Azulejo** *(Tile Museum)*
- **Aqueduto das Águas Livres** *(Águas Livres' Aqueduct)*
- **Basílica da Estrela** *(Estrela Basilica)*
- **Castelo de São Jorge** *(Saint George's Castle)*
- **Sé Patriarcal** *(Patriarchal Church)*
- **Mosteiro dos Jerónimos** *(Jerónimos Monastery)*
- **Padrão dos Descobrimentos** *(Monument to the Overseas Discoveries)*
- **Torre de Belém** *(Belém Tower)*

Map of Lisbon

linha **Azul** Blue line

linha **Amarela** Yellow line

linha **Verde** Green line

linha **Vermelha** Red line

ICCB 2022

IX International Conference on Computational Bioengineering

SCIENTIFIC PROGRAM

11 - 13 April 2022

Instituto Superior Técnico | Lisbon | Portugal

Program at a Glance

Hours	Monday, **April 11th**	Tuesday, **12th April**	Wednesday, **13th April**
08:00	**REGISTRATION**		
08:30	**OPENING**		
09:00	**PARALLEL SESSION 1** **PS 1.1 – BIOMECHANICS I** **PS 1.2 – MACHINE LEARNING AND HIGH PERFORMANCE COMPUTING**	**PARALLEL SESSION 3** **PS 3.1 –** SPECIAL SESSION: **COMPUTER MODELLING FOR TISSUE ENGINEERING APPLICATIONS I** **PS 3.2 – BIOMECHANICAL IMAGING AND VISUALIZATION**	**PARALLEL SESSION 5** **PS 5.1 –** SPECIAL SESSION: **COMPUTER MODELLING FOR TISSUE ENGINEERING APPLICATIONS II** **PS 5.2 –** SPECIAL SESSION: **COMPUTATIONAL BEHAVIOUR OF BIO-DESIGNED IMPLANTS**
09:30			
10:00			
10:30	*Coffee Break*	*Coffee Break*	*Coffee Break*
11:00	**PLENARY I** *Harry Van Lenthe* *Grace O'Connell*	**PLENARY III** *John Rasmussen* *Lorena Diéguez*	**PLENARY IV** *John Dunlop* *Laoise McNamara*
11:30			
12:00			
12:30	*Lunch*	*Lunch*	*Lunch*
13:00			
13:30			
14:00	**PARALLEL SESSION 2** **PS 2.1 – BIOMECHANICS II** **PS 2.2 –** SPECIAL SESSION: **IN SILICO CLINICAL TRIALS FOR CARDIOVASCULAR MEDICINE I**	**PARALLEL SESSION 4** **PS 4.1 – BIOMECHANICS III** **PS 4.2 –** SPECIAL SESSION: **IN SILICO CLINICAL TRIALS FOR CARDIOVASCULAR MEDICINE II**	**PARALLEL SESSION 6** **PS 6.1 –** SPECIAL SESSION: **MULTISCALE AND HETEROGENEOUS MODELLING OF CARTILAGINOUS TISSUES IN HEALTH AND DISEASE** **PS 6.2 –** SPECIAL SESSION: **FROM MOLECULAR TO CONTINUUM BIOMECHANICS / MULTIPHYSICS**
14:30			
15:00			
15:30	*Coffee Break*		***Farewell*** *(Porto Wine)*
16:00	**PLENARY II** *Scott Hollister*	***Social Program and Dinner***	
16:30			
17:00	***Welcome Reception***		
17:30			
18:00			
18:30			
19:00			
19:30			
20:00			
20:30			
21:00			
21:30			

PLENARY LECTURES I			Monday, **April 11th • 11:00-12:30**
ROOM ***MA***		CHAIR ***Ralph Muller***	**PLENARY I**
TIME	**ID**	**PLENARY SPEAKER**	**TITLE**
11:00		*Harry Van Lenthe*	**COMPUTATIONAL BIOMECHANICS FOR CLINICAL DECISION MAKING. HAVE WE REACHED IT?** *Harry Van Lenthe*
11:45		*Grace O'Connell*	**3D MODELING OF THE INTERVERTEBRAL DISC: DIRECT RELATIONSHIP BETWEEN TISSUE COMPOSITION AND MODEL PARAMETERS** *Grace O'Connell*

PLENARY LECTURES II			Monday, **April 11th • 16:00-16:45**
ROOM ***MA***		CHAIR ***Hélder C. Rodrigues***	**PLENARY II**
TIME	**ID**	**PLENARY SPEAKER**	**TITLE**
16:00		*Scott Hollister*	**FINITE ELEMENT CONTINUUM DAMAGE MODELING OF SKIN OVER AURICULAR IMPLANTS** *Scott J. Hollister*

PARALLEL SESSION 1			Monday, **April 11th • 9:00-10:30**
ROOM *02.1*		CHAIR *André Castro*	**PS 1.1 – BIOMECHANICS I**
TIME	**ID**	**PRESENTING AUTHOR**	**TITLE**
9:00	43	*Ana Guerra*	**COMPUTATIONAL METHODS TO SIMULATE SPROUTING ANGIOGENESIS - NUMERICAL ANALYSIS WITH EXPERIMENTAL VALIDATION** *Ana Guerra, Jorge Belinha, Naside Mangir, Sheila MacNeil, Renato Natal Jorge*
9:15	26	*Mariana Rodrigues da Silva*	**A NEW MODEL TO STUDY THE TALOCRURAL-TALOCALCANEAL ARTICULAR COMPLEX OF THE HUMAN FOOT** *Mariana Rodrigues da Silva, Filipe Marques, Miguel Tavares da Silva, Paulo Flores*
9:30	28	*André Filipe Geraldes Mourato*	**NUMERICAL MODELING OF THE ASCENDING THORACIC AORTA: A SYSTEMATIC REVIEW ON COMPUTATIONAL APPROACHES AND CHALLENGES TOWARDS THE CLINICAL PRACTICES** *André Filipe Geraldes Mourato, Rodrigo Valente, Moisés Brito, José Xavier, António Tomas, Stephane Avril*
9:45	29	*Jan Spicka*	**ON THE DEVELOPMENT OF A NEW VEHICLE SAFETY SYSTEM FOR A STANDARD AND NON-STANDARD SEATING CONFIGURATIONS** *Jan Spicka, Abbas Talimian, Ludek Hyncik, Tomasz Bonkowski, Petra Kochova, Alojz Hanuliak, Ludek Kovar*
10:00	44	*Maria Augusta Neto*	**STABILITY OF TWO INTERNAL FIXATION IMPLANTS IN THE TREATMENT OF FEMUR FRACTURES: EXPERIMENTAL AND FINITE ELEMENT ANALYSIS** *V. Maranha, M. A. Neto, L. M. Roseiro, M. Paulino, A. M. Amaro*
10:15	48	*José Alejandro Guerrero-Vargas*	**BIOMECHANICAL RESPONSE OF THE LUMBOSACRAL REGION L4-S1 DURING STANDING, FLEXION, AND EXTENSION MOVEMENTS, CONSIDERING THE TRABECULAR/CORTICAL BONE RATIO IN THE VERTEBRAL BODY: A FINITE ELEMENT ANALYSIS** *José Alejandro Guerrero-Vargas, Pablo Sanchez-Quinones, Humberto Madriñan-Navia, Leonardo Laverde-Frade*

PARALLEL SESSION 1			Monday, **April 11th • 9:00-10:30**
ROOM *02.2*		CHAIR *Carlos Quental*	**PS 1.2 – MACHINE LEARNING AND HIGH PERFORMANCE COMPUTING**
TIME	**ID**	**PRESENTING AUTHOR**	**TITLE**
9:00	38	*Francisco Correia Marques*	**PERFORMANCE COMPARISON OF DEEP LEARNING SEGMENTATION MODELS ON HISTOLOGICAL SECTIONS IN A MURINE BONE ADAPTATION AND REGENERATION MODEL** *Francisco Correia Marques, Patricia Schmid, Esther Wehrle, Ralph Mueller*
9:15	66	*Gauthier Dot*	**AUTOMATIC CEPHALOMETRIC LANDMARKING OF CRANIOMAXILLOFACIAL COMPUTED TOMOGRAPHY SCANS USING A COARSE-TO-FINE DEEP LEARNING APPROACH** *Gauthier Dot, Shaole Chang, Philippe Rouch, Thomas Schouman, Laurent Gajny*
9:30	76	*Matteo Bovio*	**AUTOMATIC SEGMENTATION OF THE SPINE AND LOWER LIMBS BASED ON DEEP LEARNING IN LOW-DOSE BIPLANAR RADIOGRAPHS** *Matteo Bovio, Wafa Skalli, Guillaume Rebeyrat, Ayman Assi, Laurent Gajny*
9:45	59	*Chlöe Schooling*	**TENSOR ELECTRICAL IMPEDANCE MYOGRAPHY OF THE TONGUE IN AMYOTROPHIC LATERAL SCLEROSIS IDENTIFIES THE IMPEDANCE SIGNATURE OF DISEASE PROGRESSION** *Chlöe Schooling*
10:00	27	*Luděk Hynčík*	**ON DEVELOPING SUBJECT-SPECIFIC HUMAN BODY MODELS FOR CLINICAL AND INDUSTRIAL APPLICATIONS** *Ludkěk Hynčík, Hana Čechová, Tomasz Bońkowski*

PARALLEL SESSION 2			Monday, **April 11th • 14:00-15:30**
ROOM *02.1*		CHAIR *Antonio Boccaccio*	**PS 2.1 – BIOMECHANICS II**
TIME	**ID**	**PRESENTING AUTHOR**	**TITLE**
14:00	56	*Rodrigo Baptista Valente*	**FINITE ELEMENTS ANALYSIS OF THE STRESS DISTRIBUTION ON TEMPOROMANDIBULAR JOINT DUE TO THE USE OF MANDIBULAR ADVANCEMENT DEVICES** *Rodrigo Baptista Valente, André Filipe Geraldes Mourato, Moisés Gonçalo de Brito, José Manuel Cardoso Xavier, António Cruz Tomas, Stephane Avril*
14:15	58	*João Paulo Carmo*	**PIEZOELECTRIC SENSORS INSOLE FOR ANALYSIS AND IDENTIFICATION GAIT CHARACTERISTICS** *Melkzedekue de Moraes Alcântara Calabrese Moreira, Igor Nazareno Soares, Denis César Mosconi Pereira, Gabriel Augusto Ginja, Tiago Matheus Nordi, Ruy Alberto Corrêa Altafim, Ruy Alberto Pisani Altafim, Adriano Almeida Gonçalves Siqueira, João Paulo Pereira do Carmo*
14:30	64	*Lucie Hucke*	**EFFECTS OF TENSION BAND IMPLANTS ON THE MECHANICAL LOADING OF THE FEMORAL GROWTH PLATE DURING GUIDED GROWTH IN ADOLESCENTS** *Lucie Hucke, Andreas Wittek, Jana Holder, Stefan Van Drongelen, Antonio Juan Gamez Lopez, Armin Huß*
14:45	71	*Amaury Guillermin*	**NEW APPROACH TO STUDY SKIN VISCOELASTIC THROUGH SURFACE WAVE PROPAGATION, USING NON DESTRUCTIVE IN VIVO TESTING** *Amaury Guillermin, Robin Chatelin, Eric Feulvarch, Hassan Zahouani*
15:00	87	*Rui B. Ruben*	**TRACHEOBRONCHIAL STENTS PERFORMANCE ANALYSIS** *Jairson C. Dinis, João Brites Pinto, Mário S. Correia, Henrique Almeida, Carlos A. Campos, Rui B. Ruben*
15:15	94	*Carlos Rodrigues*	**UNSUPERVISED HIERARCHICAL AND NON-HIERARCHICAL CLUSTERING TECHNIQUES ON BIOMECHANICAL VARIABLES FOR LONG AND SHORT COUNTERMOVEMENT COMPARISON WITH NO COUNTERMOVEMENT** *Carlos Rodrigues, Miguel Correia, João Abrantes, Marco Benedetti, Jurandir Nadal*

PARALLEL SESSION 2			Monday, **April 11th • 14:00-15:30**
ROOM *02.2*		CHAIR *Nenad Filipovic*	**PS 2.2 –** SPECIAL SESSION: **IN SILICO CLINICAL TRIALS FOR CARDIOVASCULAR MEDICINE I**
TIME	**ID**	**PRESENTING AUTHOR**	**TITLE**
14:00	36	*Ana Moita*	**FLUID FLOW OF BIOMIMETIC FLUIDS IN COMPLEX MICROCHANNELS FOR MICROCIRCULATION STUDIES** *Ana Moita, Inês Gonçalves, João Varelas, Rui Lima, António Luis Moreira*
14:15	78	*Milos Anic*	**NUMERICAL SIMULATIONS OF STANDARD MECHANICAL TESTS FOR THE DEVELOPMENT AND OPTIMIZATION OF FULLY BIORESORBABLE STENTS** *Miloš Anić, Miljan Milošević, Bogdan Milićević, Dalibor Nikolic, Miloš Kojić, Nenad Filipović*
14:30	80	*Nenad Filipovic*	**SILICOFCM PLATFORM, CARDIOMYOPATHY AND ELECTROMECHANICAL COUPLING** *Nenad Filipovic, Igor Saveljic, Bogdan Milicevic, Miljan Milosevic, Milos Kojic*
14:45	25	*Tim Meyer*	**ENGINEERED HEART MUSCLE FROM 3D PRINTED FIBERS** *Tim Meyer*
15:00	72	*Andjela Blagojevic*	**AGENT-BASED MODEL AND SIMULATION OF ATHEROSCLEROTIC PLAQUE PROGRESSION** *Andjela Blagojevic, Tijana Sustersic, Nenad Filipovic*

PLENARY LECTURES III			Tuesday, April 12th • 11:00-12:30
ROOM *MA*		CHAIR *Jorge Ambrósio*	PLENARY III
TIME	ID	PLENARY SPEAKER	TITLE
11:00		*John Rasmussen*	**STATISTICAL BIOMECHANICAL MODELS: FROM INDIVIDUALS TO POPULATIONS** *John Rasmussen*
11:45		*Lorena Diéguez*	**MICROFLUIDICS AND NANOTECHNOLOGY: TOWARDS ADVANCED ORGAN-ON-A-CHIP SYSTEMS** *Lorena Diéguez*

PARALLEL SESSION 3			Tuesday, April 12th • 9:00-10:30
ROOM *02.1*		CHAIR *Sara Checa/Pasquale Vena*	PS 3.1 – SPECIAL SESSION: COMPUTER MODELLING FOR TISSUE ENGINEERING APPLICATIONS I
TIME	ID	PRESENTING AUTHOR	TITLE
9:00	30	*Mahdi Jaber*	GYROID VS STRUT-LIKE SCAFFOLDS FOR BONE REGENERATION: AN IN SILICO COMPARITIVE ANALYSIS OF HEALING IN LARGE BONE DEFECTS *Mahdi Jaber, Sara Checa, Georg Duda*
9:15	33	*Luca D'Andrea*	MECHANICAL PROPERTIES OF BONE TISSUE ENGINEERING BIOCERAMIC SCAFFOLDS ASSESSED THROUGH MICRO-CT BASED FINITE ELEMENT MODELS *Luca D'Andrea, Dario Gastaldi, Francesco Baino, Enrica Verné, Martin Schwentenwein, Thomas Prochaska, Pasquale Vena*
9:30	46	*Antonio Boccaccio*	GEOMETRY OPTIMIZATION OF REGULAR SCAFFOLDS FOR BONE TISSUE ENGINEERING: A MECHANOBIOLOGICAL APPROACH *Óscar Libardo Rodríguez-Montaño, Carlos Julio Cortés-Rodríguez, Lorenzo Vaiani, Antonio Boccaccio*
9:45	52	*Chiara Dazzi*	THE ROLE OF INTRINSIC AND EXTRINSIC MECHANICS ON ENDOTHELIAL CELLS AND FIBROBLASTS ORGANIZATION DURING EARLY BONE HEALING: AN IN SILICO STUDY *Chiara Dazzi, Julia Mehl, Georg N. Duda, Sara Checa*
10:00	57	*Marius Zeinhofer*	RAPID, PATIENT SPECIFIC OPTIMIZATION OF BONE SCAFFOLDS *Patrick Dondl, Marius Zeinhofer*
10:15	63	*Hygor P. M. Melo*	COMBINING EXPERIMENTS AND IN SILICO MODELING TO INFER THE ROLE OF ADHESION AND PROLIFERATION ON THE COLLECTIVE DYNAMICS OF CELLS *Hygor P. M. Melo, Fatima R. Maia, André S. Nunes, Rui L. Reis, Joaquim M. Oliveira, Nuno A. M. Araújo*

PARALLEL SESSION 3			Tuesday, April 12th • 9:00-10:30
ROOM *02.2*		CHAIR *Rui Ruben*	PS 3.2 – BIOMECHANICAL IMAGING AND VISUALIZATION
TIME	ID	PRESENTING AUTHOR	TITLE
9:00	40	*Carolin Vosseler*	IMPLEMENTATION OF A MICROSOFT HOLOLENS 2 FOR SUPPORTING DIAGNOSIS AND MONITORING TREATMENT OF SCOLIOSIS *Kirstin Krueger, Carolin Vosseler, Xhensila Lakti, Radu Emanuil Petruse, Saša Ćuković, Gerrit Meixner*
9:15	81	*Francisco Caramelo*	REALISTIC 3D PHOTO-RECONSTRUCTION FROM CBCT IMAGES *Miguel Monteiro, Inês Francisco, Nuno Ferreira, Francisco Vale, Francisco Caramelo*
9:30	82	*Xhoena Polisi*	CLASSIFICATION OF CELL BIOMATERIAL INTERACTION TOXICITY LEVEL USING CONVOLUTIONAL NEURAL NETWORKS *Xhoena Polisi, Edit Dollani, Arban Uka*
9:45	60	*Meredith Ellis*	A MATHEMATICAL HOMOGENISATION APPROACH TO MASS TRANSPORT MODELS FOR ORGANOID CULTURE *Meredith Ellis, Sarah Waters, Helen Byrne, Mohit Dalwadi, Marianne Ellis, William Newell*

PARALLEL SESSION 4			Tuesday, **April 12th • 14:00-15:30**
ROOM *02.1*		CHAIR *João Folgado*	**PS 4.1 – BIOMECHANICS III**
TIME	**ID**	**PRESENTING AUTHOR**	**TITLE**
14:00	96	*Ivo Fialho Roupa*	**IMPLEMENTATION OF A 2D MUSCULOSKELETAL MODEL FOR THE ANALYSIS OF HUMAN MOVEMENT USING FULLY CARTESIAN COORDINATES** *Ivo Fialho Roupa, Rita Peneque, Sérgio B. Gonçalves*
14:15	100	*Gonçalo Marta*	**PREDICTION OF GROUND REACTION FORCES DURING RUNNING** *Gonçalo Marta, João Folgado, Carlos Quental, Francisco Guerra Pinto*
14:30	101	*Madalena Antunes*	**GRAFT POSITIONING IN SUPERIOR CAPSULAR RECONSTRUCTION: COMPUTATIONAL ANALYSIS OF GRAFT INTEGRITY AND SHOULDER STABILITY** *Madalena Antunes, Carlos Quental, João Folgado, Clara de Campos Azevedo, Ana Catarina Ângelo*
14:45	105	*Zakaria Meddings*	**THE INFLUENCE OF HYPER-ELASTIC MATERIAL PROPERTIES ON MECHANICAL STRESS IN CAROTID ARTERY PLAQUES: A 3D STRUCTURAL SIMULATION ROBUSTNESS STUDY"** *Zakaria Meddings*
15:00	110	*Jorge Ambrósio*	**INVERSE DYNAMICS APPROACH TO THE BIOMECHANICS OF SWIMMERS USING MULTIBODY DYNAMICS METHODOLOGIES** *Jorge Ambrósio, Francisca Simões, Mariana Sequeira, Carlos Quental, João Paulo Vilas-Boas*
15:15	89	*Abdul Aziz Vaqar*	**EFFECT OF TOTAL HIP ARTHROPLASTY ON HIP RANGE OF MOTION AND ASSOCIATED MUSCLE FORCES** *Abdul Aziz Vaqar, Kinda Khalaf, Maher Maalouf, Tao Liu, Marwan El Rich*

PARALLEL SESSION 4			Tuesday, **April 12th • 14:00-15:30**
ROOM *02.2*		CHAIR *Nenad Filipovic*	**PS 4.2 –** SPECIAL SESSION: **IN SILICO CLINICAL TRIALS FOR CARDIOVASCULAR MEDICINE II**
TIME	**ID**	**PRESENTING AUTHOR**	**TITLE**
14:00	73	*Nevena Milivojević*	**NOVEL APPROACH IN DESIGNING MICROFLUIDIC DEVICES BASED ON FINITE ELEMENT AND TOPOLOGICAL OPTIMISATION METHODS** *Nevena Milivojević, Dalibor Nikolić, Marko Živanović, Nenad Filipović*
14:15	74	*Smiljana Tomasevic*	**ANALYSIS OF CARDIAC WORK AND SIMULATION OF AORTIC VALVE STENOSIS** *Smiljana Tomasevic, Bogdan Milicevic, Igor Saveljic, Lazar Velicki, Nenad Filipovic*
14:30	61	*Tijana Sustersic*	**TOWARDS FULLY AUTOMATED 3D RECONSTRUCTION OF HEART - SEGMENTATION AND PARAMETRIC HEART MODEL OF PATIENTS WITH CARDIOMYOPATHY** *Tijana Sustersic, Andjela Blagojevic, Bogdan Milicevic, Miljan Milosevic, Nenad Filipovic*
14:45	69	*Dalibor Nikolic*	**IN-SILICO TOOL FOR VIRTUAL HEMODYNAMICS OF FEMORO-POPLITEAL "BI-PASS" SURGERY** *Dalibor D. Nikolic, Dragan B. Sekulic, Danko Z. Milasinovic, Dragana S. Paunovic, Igor M. Sekulic, Igor B. Saveljic, Nenad D. Filipovic*
15:00	70	*Bogdan Milićević*	**SIMULATION OF THE FULL CARDIAC CYCLE USING PARAMETRIC LEFT VENTRICLE MODEL** *Bogdan Milićević, Miljan Milošević, Vladimir Simić, Miloš Kojić, Nenad Filipović*

PLENARY LECTURES IV			Wednesday, **April 13th • 11:00-12:30**
ROOM *MA*		CHAIR *Dominique Piolleti*	**PLENARY IV**
TIME	**ID**	**PLENARY SPEAKER**	**TITLE**
11:00		*John Dunlop*	**MODELLING THE ROLE OF CURVATURE ON TISSUE PATTERNING AND GROWTH** *John W. C. Dunlop, Barbara Schamberger, Andreas Roschger, F. Dieter Fischer, Peter Fratzl*
11:45		*Laoise McNamara*	**COMPUTATIONAL MODELLING TO ADVANCE UNDERSTANDING OF HOW MEDICAL DEVICE DESIGN INFLUENCES THE CELLULAR BIOPHYSICAL ENVIRONMENT** *Laoise McNamara*

PARALLEL SESSION 5			Wednesday, **April 13th • 9:00-10:30**
ROOM *02.1*		CHAIR *Sara Checa/Pasquale Vena*	**PS 5.1 –** SPECIAL SESSION: **COMPUTER MODELLING FOR TISSUE ENGINEERING APPLICATIONS II**
TIME	**ID**	**PRESENTING AUTHOR**	**TITLE**
9:00	65	***Cristovão Dias***	**MODELLING OF CELL-MEDIATED SELF-ASSEMBLED COLLOIDAL SCAFFOLDS** *C. S. Dias, C. A. Custódio, G. C. Antunes, M. M. Telo da Gama, J. F. Mano, N. A. M. Araújo*
9:15	75	***João Meneses***	**BIOREACTOR DIGITAL TWIN - AN ESSENTIAL MODELLING TOOL TO ESTIMATE LOCAL CELLULAR ENVIRONMENTAL CONDITIONS IN EXPERIMENTAL TISSUE ENGINEERING.** *João Meneses, João Silva, Nuno Alves, Tiago Santos, Pedro Cavaleiro Miranda, Paula Pascoal Faria*
9:30	77	***Nicolás Laita***	**EXPERIMENTAL AND COMPUTATIONAL FRAMEWORK TO DESIGN WELL-ORGANIZED FIBROUS SCAFFOLDS FOR CARDIAC TISSUE ENGINEERING** *Nicolás Laita, Gerardo Cedillo-Servin, Andrei Hrynevich, Miguel Ángel Martínez, Miguel Castilho, Manuel Doblaré, Estefanía Peña*
9:45	83	***João Carlos Silva***	**EFFECTS OF ELECTRICAL STIMULATION CONDITIONS ON HUMAN MESENCHYMAL STEM/STROMAL CELLS OSTEOGENIC DIFFERENTIATION: REFINING PROTOCOLS TOWARDS ENHANCED IN VITRO BONE FORMATION** *João Carlos Silva, João Meneses, Fábio Garrudo, Nuno Alves, Frederico Ferreira, Paula Pascoal-Faria*
10:00	113	***Tiago Pires***	**PERMEABILITY AND WALL SHEAR STRESS ANALYSIS IN SMOOTHED VS NON-SMOOTHED TPMS SCAFFOLDS** *T. H. V. Pires, A. P. G. Castro e P. R. Fernandes*
10:15	112	***Jorge E. Santos***	**TPMS SCAFFOLDS FOR BONE-CARTILAGE INTERFACE** *J. E. Santos, P. S. Martins, P. R. Fernandes, A. P. G. Castro*

PARALLEL SESSION 5			Wednesday, **April 13th • 9:00-10:30**
ROOM *02.2*		CHAIR *António Ramos*	**PS 5.2 –** SPECIAL SESSION: **COMPUTATIONAL BEHAVIOUR OF BIO-DESIGNED IMPLANTS**
TIME	**ID**	**PRESENTING AUTHOR**	**TITLE**
9:00	86	***Dominique P. Pioletti***	**DEVELOPMENT OF CUSTOMIZED COMPOSITE MOUTHGUARDS TO IMPROVE ATHLETES SAFETY AND COMPLIANCE** *Naser Nasrollahzadeh, Martin Broome, Dominique P. Pioletti*
9:15	41	***Lidia Carvalho***	**NUMERICAL EVALUATION OF THE PERMEABILITY OF IMPLANT WITH POROUS STRUCTURE** *Lídia Carvalho*
9:30	42	***Lidia Carvalho***	**NUMERICAL IMPLEMENTATION OF THE POLYLACTIC ACID (PLA) BEHAVIOUR DURING IMPLANT DEGRADATION** *Lídia Carvalho*
9:45	85	***António Ramos***	**PERDITION OF LOAD TRANSFER IN BIOINSPIRED CONCEPTS FOR BONE IMPLANT INTERFACE, A FINITE ELEMENT STUDY** *António Ramos, Gabriel Ribeiro, Lidia Carvalho, Michel Mesnard*
10:00	32	***Cátia Gomes***	**BIOINSPIRED DENTAL IMPLANT CONCEPT, A FINITE ELEMENT STUDY** *Cátia Gomes, Michel Mesnard, António Ramos*

PARALLEL SESSION 6			Wednesday, April 13th • 14:00-15:30
ROOM *02.1*		CHAIR *Jérôme Noailly*	**PS 6.1 –** SPECIAL SESSION: **MULTISCALE AND HETEROGENEOUS MODELLING OF CARTILAGINOUS TISSUES IN HEALTH AND DISEASE**
TIME	**ID**	**PRESENTING AUTHOR**	**TITLE**
14:00	99	*Estefano Muñoz-Moya*	**TOWARDS A REPOSITORY OF PATIENT-SPECIFIC INTERVERTEBRAL DISCS FINITE ELEMENT MODELS** *Estefano Muñoz-Moya, Morteza Rasouligandomani, Carlos Ruiz Wills, Gemma Piella, Jérôme Noailly*
14:15	98	*Sofia Tseranidou*	**NETWORK MODELLING FOR NUCLEUS PULPOSUS CELL ACTIVITY IN EARLY INTERVERTEBRAL DISC DEGENERATION** *Sofia Tseranidou, Maria Segarra-Queralt, Janet Piñero, Jérôme Noailly*
14:30	108	*Dimitrios Lialios*	**AN HPC APPLICATION OF PORO-ANISO-HYPERELASTIC MODEL FOR THE IN SILICO STUDY OF THE INTERVERTEBRAL DISC DEGENERATION** *Dimitrios Lialios, Mariano Vázquez, Beatriz Eguzkitza, Eva Casoni, Jérôme Noailly*
14:45	67	*Laura Baumgartner*	**INTEGRATION OF MECHANICAL STIMULI INTO AGENT-BASED SIMULATIONS OF INTERVERTEBRAL DISC CELL ACTIVITY** *Laura Baumgartner, Miguel Ángel González Ballester, Jérôme Noailly*
15:00	68	*Maria Segarra-Queralt*	**MECHANOTRANSDUCTION COMPUTATIONAL APPROACH OF CHONDROCYTES** *Maria Segarra-Queralt, Gemma Piella, Jérôme Noailly*

PARALLEL SESSION 6			Wednesday, April 13th • 14:00-15:30
ROOM *02.2*		CHAIR *Christian Hellmich*	**PS 6.2 –** SPECIAL SESSION: **FROM MOLECULAR TO CONTINUUM BIOMECHANICS / MULTIPHYSICS**
TIME	**ID**	**PRESENTING AUTHOR**	**TITLE**
14:00	47	*Christian Hellmich*	**COMPLEX BIOMECHANICS: EMERGENT PATTERNS FROM ATOMS TO PATIENTS** *Stefan Scheiner, Niketa Ukaj, Johannes Kalliauer, Christian Hellmich*
14:15	53	*Ted Vaughan*	**A MULTISCALE MODEL INVESTIGATING THE ROLES OF MINEARLISED COLLAGEN FIBRILS AND THE EXTRA-FIBRILLAR MATRIX ON BONE BIOMECHANICS** *Ted Vaughan, Hamid Alijani, Mahdi Tavakol*
14:30	31	*Malwina Matella*	**A MULTISCALE FINITE ELEMENT MODEL OF THE ELECTRICAL PROPERTIES OF THYROID TISSUE** *Malwina Matella, Dawn Walker, Keith Hunter*
14:45	106	*Vincent Casey*	**TISSUE THERMAL DAMAGE IS REDUCED WHEN USING INSULATED ELECTRODES IN COMPARISION TO STANDARD ELECTRODES DURING ELECTROSURGERY: A COMPUTATIONAL INVESTIGATION** *Vincent Casey, Elzbieta Ewertowska, Micheal Burke, Laura Frey, Paul Sheridan, Ben Row, Bryan Deeny, Laoise McNamara*
15:00	107	*Elzbieta Ewertowska*	**NUMERICAL ANALYSIS OF SINGLE AND MULTI-FREQUENCY CURRENT WAVEFORMS AND THE EFFECT OF OPEN-IRRIGATION COOLING DURING BIPOLAR ELECTROSURGERY** *Elzbieta Ewertowska, Vincent J. Casey, Micheal Burke, Kenneth O'Mahony, Laoise M. McNamara*

ICCB 2022

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BOOK OF ABSTRACTS

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Plenary Lecture

COMPUTATIONAL BIOMECHANICS FOR CLINICAL DECISION MAKING. HAVE WE REACHED IT?

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Summary: Computational models are widely used in medical sciences to study disease aetiology and progression. Finite element analysis is one specific computational modeling technique, widely used for the mechanical evaluation and characterization of objects and with applications across all length scales. Since its first application to biological tissues 50 years ago [1], its use has increased tremendously. Whereas initial analyses dealt with concepts, and with improving devices such as total hip replacements, the tremendous increase in computational power has brought more detail and more physiological accuracy into the models, thus allowing patient-specific/specimen-specific analyses. These analysis have demonstrated that accurate estimates of stiffness, strength and deformation behavior of biological tissues such as bones and bone-implant structures can be obtained; i.e., many studies have appeared in which finite element modelling has been used to quantify mechanical performance, and how these properties change with specific treatment. Though implementation of this technique in a clinical context seems a logical and straight-forward step, this has seen only very few actual realizations. Why? What are the hurdles? In this presentation I will address these questions. As an example I will show that finite element analysis can provide a biomechanics-based evaluation of the risk for bone fracture in patients with bone tumors, before and after treatment. These data can support clinicians in the decision process. At the same time it remains a challenge to include additional factors related to patients health status and well-being and to weigh the impact of treatment.

References

[1] Brekelmans, Poort, and Slooff (1972), Acta *Orthop*. Scand. 43: 301-317

Plenary Lecture

3D MODELING OF THE INTERVERTEBRAL DISC: DIRECT RELATIONSHIP BETWEEN TISSUE COMPOSITION AND MODEL PARAMETERS

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Keywords: finite element modeling, intervertebral disc, multi-scale mechanics

Summary: Age and disease cause significant changes in intervertebral disc composition, resulting in altered mechanical function that may lead to debilitating lower back pain. *In vitro* cadaveric tissue testing has played a crucial role in the understanding spine biomechanics. However, clinical relevance of *in vitro* tests has been limited due to many factors that can introduce artifacts into the data and outcomes.[1] Computational models provide a powerful tool to supplement experimental data, but most models are limited to describing tissue behavior under the loading modality or condition (*e.g.*, healthy or degenerated) used for model calibration. We developed a multi-scale structure-based modeling framework where model parameters are based on sub-tissue level composition, including water and glycosaminoglycan content and collagen fibril stiffness. The model was capable of accurately predicting joint-level mechanics and morphological changes observed with degeneration.

Finite element models were developed using the FEBio computational suite for soft tissue biomechanics. Triphasic material descriptions were used to simulate tissue swelling and account for changes in glycosaminoglycan content with age and degeneration. Models of the annulus fibrosus (AF) and nucleus pulposus (NP) were initially developed to perform model validation on multiple length scales by comparing model predicted mechanics to tissue-level data in the literature. Then, bone-disc-bone models were developed and validated by comparing model-predicted joint-level mechanics to data in the literature. Finally, the validated model was used to study risk of herniation by simulating a wide range of compression with flexion, which has been thought to increase risk of herniation.[2]

16 tissue-level simulations and 13 joint-level simulations were performed for model validation. The model closely matched data in the literature for 26 of 29 cases. Thus, we considered the multi-scale model development framework to be valid for simulating both tissue- and joint-level disc mechanics. Flexion was assessed by moving the center of rotation to better represent changes in rotation based on various physical activities. These simulations showed that torque-based flexion commonly used for *in vitro* experiments hadminimal risk for herniation or disc failure. In contrast, shifting the axis of rotation anteriorly, which is more representative of *in vivo* muscle-based flexion, greatly increased the risk of herniation in locations that are commonly observed clinically. Multi-scale structure-based modeling has the potential to accurately describe and predict disc joint failure that will be important for improving surgical outcomes following fusion or disc replacement.

References

[1] Costi JC, Ledet E, O'Connell GD, Spine Biomechanical Testing Methodologies: The Controversy of Consensus vs Scientific Evidence, JOR Spine,2021.

[2] Berger-Roscher N, Casaroli G, Rasche V, Villa T, Galbusera F, Wilke HJ, Influence of Complex Loading Conditions on Intervertebral Disc Failure, Spine,2017

Plenary Lecture

FINITE ELEMENT CONTINUUM DAMAGE MODELING OF SKIN OVER AURICULAR IMPLANTS

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Summary: We hypothesize the increased strain on skin over an auricular scaffold constricts blood flow leading to adverse remodeling of skin extracellular matrix. In addition, increased skin strain may also cause direct structural damage. We further hypothesize that location of both the vascular remodeling and direct structural damage may be predicted using isotropic Continuum Damage modeling, where damage is characterized by a scalar parameter D that varies from 0 (no damage) to 1 (complete failure). We utilized the Simo Reactive Damage Mechanics model $D\left(\sigma_f, time\right) = 1 - \frac{a}{\sigma_f}\left(1 - e^{-\frac{\sigma_f}{a}}\right)$ in FEBio to predict damage distribution in an idealized skin stretched over an ear implant, where a is a constitutive parameter chosen as 15 MPa to match the failure stress of rat skin reported by Haut[1]. The reactive damage constitutive model reduces the material elastic properties as damage accumulates: $W = \left(1 - D\right)W_0$. Two types of PCL ear scaffolds were modeled, a solid implant and a 59% porous implant with spherical pores. The ear scaffold was pushed into the skin to model surgical implantation to a depth of 26mm, assuming frictional sliding elastic contact occurred between skin and scaffold.

We further modeled scaffold modifications used to potentially mitigate skin damage. These scaffold modifications included 1) reducing the overall scaffold stiffness from PCL to that of auricular cartilage[2], 2) placing tissue cylindrical tissue biopsies in between the skin and scaffold, and 3) creating a form fitting helix cushion between the scaffold and skin.

Results for both the solid and 59% porous PCL scaffolds showed the highest damage results (up to 0.2) over the superior and lateral areas of the helix. These damage locations correlate with skin dehiscence locations over implanted ear scaffolds in a rat model[3]. Of the various mitigation strategies, significantly reducing the scaffold stiffness to match that of auricular cartilage was most effective in reducing damage. However, reducing the scaffold stiffness to that of auricular cartilage[2] leads to significant scaffold deformation and loss of shape, which defeats the purpose of creating a scaffold to reconstruct facial aesthetics. One compromise is the use of a thinner soft material in between the stiffer aesthetic stiffer scaffold and the skin. This stiffness gradient would reduce stress and therefore damage in the skin. Results

showed this approach could reduce accumulated skin damage between 5% and 20%. In conclusion, continuum damage modeling can be used to determine of possible dehiscence locations of skin over facial plastic scaffolds, and inform design of interventions that may mitigate skin dehiscence.

References

[1] Haut RC. The effects of orientation and location on the strength of dorsal rat skin in high and low speed tensile failure experiments. J Biomech Eng. 1989;111(2):136-40. Epub 1989/05/01. doi: 10.1115/1.3168354. PubMed PMID: 2733408.

[2] Zopf DA, Flanagan CL, Nasser HB, Mitsak AG, Huq FS, Rajendran V, Green GE, Hollister SJ. Biomechanical evaluation of human and porcine auricular cartilage. Laryngoscope. 2015;125(8):E262-8. Epub 2015/04/22. doi: 10.1002/lary.25040. PubMed PMID: 25891012; PMCID: PMC4512857.

[3] Chang B, Cornett A, Nourmohammadi Z, Law J, Weld B, Crotts SJ, Hollister SJ, Lombaert IMA, Zopf DA. Hybrid Three-Dimensional-Printed Ear Tissue Scaffold With Autologous Cartilage Mitigates Soft Tissue Complications. Laryngoscope. 2021;131(5):1008-15. Epub 2020/10/07. doi: 10.1002/lary.29114. PubMed PMID: 33022112; PMCID: PMC8021596.

Plenary Lecture

STATISTICAL BIOMECHANICAL MODELS: FROM INDIVIDUALS TO POPULATIONS

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Keywords: Biomechanics, Data Science, Running

Summary: Research into computational biomechanical models is influenced by two tendencies. On the one hand, much effort is devoted to subject-specific models, for instance a model of an orthopedic patient for the purpose of surgical planning. To this end, subject-specific data such as motion capture and medical imaging are included to improve the validity of the model. The model development process is typically laborious and can be too time-consuming for clinical use. On the other hand, computational biomechanics is inspired by rapid developments in data science, machine learning, artificial intelligence, etc., which require big data representing populations, and where the data analysis provides information about variability of parameters that separate individuals. Individualized models can then be perceived as specific parameter combinations in the population space, so the effort to make population models also serves the purpose of improving the ability to make individualized models, possibly with less laborious procedures. This presentation introduces a set of general procedures for population data processing and a versatile machine learning algorithm that produces subject-specific models based on the processed data and "little dataƒ" of subject-specific information. In brief, motion capture data is subjected to an advanced kinematic processing, which extracts anatomical angle variations and detailed anthropometric information from them. The time-series data are then Fourier-transformed to derive signal features, which are subjected to principal component analysis. The approach is illustrated by examples of virtual runners generated from the big data set. This process reveals that a runner is described by roughly 1200 parameters with strong internal correlations that enable about 90% of the variance to be described by about 50 principal components. A conditional likelihood algorithm formulated as a quadratic programming problem produces estimates of all 1200 parameters given knowledge of a subset of them. For example, the algorithm will predict a running pattern characteristic for a person with given anthropometry. The relatively strong correlation between the model parameters means that it may be possible to reconstruct complex motion data based on simple and non-invasive measurements, for instance with inertial measurement units. Population-based models also have interesting perspectives for biomechanical science. Many biomechanical investigations begin with data collection from experiments with a cohort of unspecific test subjects, i.e., the statistical distribution of the cohort is important, but the individuals are not. In relation to such cases, population-based, big-data biomechanical models can work as a virtual lab from which populations with given properties or property variations can be sampled infinitely without conducting physical experiments.

Plenary Lecture

MICROFLUIDICS AND NANOTECHNOLOGY: TOWARDS ADVANCED ORGAN-ON-A-CHIP SYSTEMS

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Keywords: cancer, metastasis, liquid biopsy, microfluidics, nanobiosensors, organ-on-a-chip

Summary: Cancer is a leading cause of morbidity and mortality worldwide. Early dissemination of cancer is difficult to detect by traditional imaging and pathological methods. While the presence of cancer material in body fluids is well known, current techniques for the isolation, analysis and characterization of these biomarkers are not efficient enough to be fully applied in clinical routine. Microfluidics presents numerous advantages for the handling of biological samples, as it provides careful control of fluids in the microscale. When it comes to biomarkers enrichment, microfluidics has demonstrated superior sensitivity and enhanced recovery compared to traditional methods. Nanobiosensors, on the other hand, offer efficient and multiplex characterization of biological entities from complex matrices, making lab-on-a-chip technologies ideal for field applications, enabling high throughput, portability, and automation in real settings. Furthermore, the development of biomimetic tumor models incorporating patient-derived material, might provide valuable information to assess the different stages of cancer, as well as to design personalised treatments. In this talk, we present our most recent work for integrated isolation and analysis of multiple circulating biomarkers, their incorporation in tumor models, and their validation in clinical settings.

Plenary Lecture

MODELLING THE ROLE OF CURVATURE ON TISSUE PATTERNING AND GROWTH

John W. C. Dunlop[1], Barbara Schamberger[1], Andreas Roschger[1], F. Dieter Fischer[2], Peter Fratzl[3]
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Keywords: Tissue Growth, Modelling, Curvature

Summary: It is well known that the physical environment of growing cells and tissues plays an important role on their behaviour. In particular recent research has shown that the curvature of a substrate can influence the growth of a tissue and also the organisation of the extracellular matrix that is produced by the cells. In this presentation we will use theoretical tools to explore experimental data of bone-like tissues growing on surfaces of constant mean curvature. Selective Plan Illumination Microscopy measurements of stained tissues show that the surface of a growing tissue closely approximates that of a Delaunay Surface. What is intriguing however is that the actin stress fibres within the tissue surface are helical and twist around the tissue surface. The helicity has similar aspects to that observed in the arrangement of collagen within and around osteons. In order to better understand this, we have developed a simple theoretical model to describe tensile fibres constrained within a fluid-like surface. The presentation will discuss aspects of this model and key questions that are still open in terms of understanding how cells can self-organise to produce complex tissues at large length scales.

Plenary Lecture

COMPUTATIONAL MODELLING TO ADVANCE UNDERSTANDING OF HOW MEDICAL DEVICE DESIGN INFLUENCES THE CELLULAR BIOPHYSICAL ENVIRONMENT

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Keywords: Medical device, Mechanobiology, Cellular, TAVR, Surgical tools

Summary: Conventional design and development efforts for medical devices largely focus on establishing biological compatibility and mechanical stability of the devices. However, biological cells and tissues respond to these biophysical stimuli imposed by medical devices by activating mechanobiological processes that can dictate cell and tissue regeneration or cell death. These responses dictate post-surgical healing and long-term performance of implanted devices, but remain poorly understood. Although computational models are widely used to predict device performance for regulatory purposes, these have not yet adequately accounted the biomechanical environment presented in vivo and how the presence of the device alters this environment. Specifically, the native geometry, tissue properties and complex multi-physics environment are critical to the interaction between biological tissues and medical devices, but are often neglected. Our research seeks to develop advanced computational modelling platforms to analyse the biophysical stimuli imposed by medical device on cells and tissues, to enable preclinical assessment of the performance of medical devices. A particular focus of our research has been to study transcatheter aortic valve replacement (TAVR) devices used to treat aortic stenosis. Although TAVR devices are widely used, there are still procedural complications associated with conventional devices that must be overcome. In particular, paravalvular leakage, interferance with the normal conductance valve migration and plaque cavitation leading to stroke can arise. These have been proposed to be associated with variances in patient anatomies, device design, malpositioning or incorrect sizing. The mechanical disturbances presented by the device likely activate biological responses in the native environment. However, there is a lack of understanding regarding the optimal positioning and appropriate sizing of TAV devices for particular patient cases to account for and mitigate such responses. Patient-specific modelling approaches allow for the reconstruction of the individual patient anatomies to predict the tissue stress after device implantation *in-vivo*. In our research we have developed realistic aortic root models by segmenting Multi-Slice Computed Tomography (MSCT) images of TAVR patients, and used these to develop finite element models of the device implantation procedure. We have applied these patient-specific models to study tracking and deployment forces during TAVR implantation, and also to investigate the design and deployment conditions associated with conductance interference and paravalvular leakage. We also strive to provide an advanced understanding of surgical devices, which provide access to organs and joints of the body and enable surgical procedures on biological tissues. Surgical drills and electrosurgical tools can induce elevated temperatures (> 100°C) in the surrounding tissue and cells, which can lead to cell death by either necrosis or apoptosis and activate cellular responses in the remaining cells. Depending on the extent of the cellular thermal

damage, cells in the damage vicinity will be either removed or recover, and this delays the healing process. Our research develops multiphysics computational models to investigate the relationship between surgical device design, operating conditions, and tissue properties and how these influence thermal elevations and the likelihood of cellular damage. This digital evidence can inform early device development and regulatory evaluation of medical devices.

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ABSTRACTS

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Abstract ID 25

ENGINEERED HEART MUSCLE FROM 3D PRINTED FIBERS

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Keywords: engineered heart muscle, 3D bioprinting, extrusion bioprinting

Summary: Cardiovascular diseases and myocardial infarction (MI) are, despite significant efforts, the leading cause of death worldwide. Recovery from MI is severely limited as heart muscle is, like neuronal tissue, non-regenerative and pharmacologic treatment may merely milden symptoms while heart transplant remains the sole cure. Engineered human myocardium (EHM) derived from bioreactor-grown human cardiomyocytes (hCM) lends itself to overcome the notorious shortage of donor hearts and in combination with 3D Bioprinting it renders personalize heart repair possible. The institute of pharmacology and toxicology has developed EHM patches that are currently undergoing clinical trials. Next generation of patches shall create well-defined and individualized force patterns to optimally support pumping function of the damaged heart (indiHEART). To achieve this goal, we shift from cast molding to 3D bioprinting using a multi-channel co-axial extrusion system to generate continuous, tubular core-shell fibers by wet-spinning and 3-D bioprinting into a sacrificial support slurry.

Abstract ID 26

A NEW MODEL TO STUDY THE TALOCRURAL-TALOCALCANEAL ARTICULAR COMPLEX OF THE HUMAN FOOT

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Keywords: Human foot, Talocrural-talocalcaneal articular complex, Foot model, Multibody dynamics

Summary: The foot is a complex structure that is adapted to allow orthograde bipedal locomotion, being the only part of the human body that is in regular contact with the ground. It comprises 28 separate bones and 31 articulations that enable the performance of several movements of the daily life. Amongst these 31 articulations, the talocrural and the talocalcaneal articulations are considered to be the focal point of this work. The talocrural articulation enables plantarflexion and dorsiflexion in the sagittal plane, and it is located between the talus of the foot and the distal ends of the tibia and fibula of the lower leg. The foot is also able to produce movement in the frontal plane, namely inversion and eversion. This motion is provided by the talocalcaneal articulation that is located between the tarsal bones of the posterior part of the foot, more specifically the calcaneus and the talus. A comprehensive inspection of the currently available scientific literature indicates that the human foot and its articulations can be modelled in distinct ways considering more or less complex approaches, which mimic more or less accurately the physiological features intrinsic to the foot. These approaches range from considering this anatomical structure as a unique segment articulating with the lower leg via the talocrural articulation to modeling the foot as a multi-segment structure with numerous articulations that enable diverse movements in different cardinal planes. However, to date, studies have not yet considered a more physiologically accurate modelling of the movements enabled by the talocrural and talocalcaneal articulations, which is a key aspect in studying the foot in clinical settings. Thus, the aim of this work is to propose a biomechanical model of the human foot incorporated with a new approach to study the talocrural-talocalcaneal articular complex. The proposed approach relies on the use of a modified type of universal joint, incorporated with a massless link assumption representing the talus. The first section of this work consists on the clear explanation of the rationale for using this new approach taking into consideration the physiological characteristics of the human foot. Then, the detailed description of the kinematic aspects associated with the formulation developed for the modified universal joint is provided. In this process, the kinematic constraint equations considered for this particular case of universal joint, along with the resultant Jacobian matrix and right-hand side of the acceleration equations are presented. The application of this new approach to the dynamic modelling and simulation of the human foot is investigated and validated against results available in the literature concerning the range of motion

permitted by the talocrural and the talocalcaneal articulations during normal gait. Subsequently, the foot model developed in this work is compared to a model available in the literature. The results obtained from the comparison of these two biomechanical models are critically discussed.

Abstract ID 27

ON DEVELOPING SUBJECT-SPECIFIC HUMAN BODY MODELS FOR CLINICAL AND INDUSTRIAL APPLICATIONS

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Keywords: subject-specific human body model, scaling, personalization, morphing

Summary: Subject-specific biomechanical models start to help engineers to design personal devices and assess injury risk and to doctors to provide patient-specific health care and treatment. As a person-specific human body model is demanding to be developed, scaling, personalization and morphing procedures apply for the necessary level of detail. All the procedures address a reference model, which is updated based on global population dimensions, global subject-specific dimensions or local subject-specific dimensions, particularly. The scaling procedure updates the global dimensions of the reference model to describe an average representative of the population group with the given anthropometry. Only the major characteristics like total height, total mass, gender and age apply. Those global parameters are applied to scale particular human body segments separately. The work shows a scaling algorithm leading to the population-based modeling to be exploited mainly for designing the generic transport safety systems. The scaling approach is the first step for personalization. Whilst scaling changes only the global dimensions based on the general population group anthropometric parameters, personalization updates the local geometrical and biomechanical details of the particular human body segments, which leads to a particular subject-specific model. Such subject-based modeling leads to personalized safety and personal protective equipment, like helmets and other protectors decreasing the injury risk from the impact. The procedure adopting the clothing patterns to develop a subject-specific human body model is presented in the study and compared to the initial scaling approach. For patient-specific modeling, a considerable level of detail must be addressed. Whilst the personalization algorithm concerns global body dimensions adopted from the clothing industry applied for the full human body, the mesh-morphing algorithm using pre-defined landmarks can be easily implemented for developing any human body segment. The presented mesh-morphing algorithm using radial basis functions to morph a template model is presented to develop a given patient-specific geometry. All three approaches are discussed from the point of view of transportation safety, personal protective equipment and person-specific health care and treatment.

Abstract ID 28

NUMERICAL MODELING OF ASCENDING AORTA ANEURYSMS: A SYSTEMATIC REVIEW ON COMPUTATIONAL APPROACHES AND CHALLENGES TOWARDS THE CLINICAL PRACTICES

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Keywords: Computational Mechanics, Ascending Thoracic Aorta Aneurysms, Biomechanics

Summary: Ascending Thoracic Aortic Aneurysms (ATAA) are one of the most common causes of mortality in developed countries. According to the European and American Guidelines for ATAA, the surgical indication is supported by the maximum diameter criterion. However, there are several reported cases of acute complications in patients with normal aortic diameters. A hypothesis can be formulated proposing a digital twin representation of aneurysms to provide a suitable platform to support clinical guidelines. This patient-specific digital platform should be built on advanced computational tools and assisted by medical-imaging data. This article presents a review, following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) methodology, concerning computational modelling of ascending aorta aneurysms enhancing challenges towards the clinical practices. The election process was performed by analyzing both title and abstract and only articles that developed biomechanical based computational models on healthy and diseased aortas were selected. A comprehensive research was performed on two databases. An analysis was developed to synthesise and uniformise the data extraction process. Contemporary evidence proves that computational models are able to provide clinicians with additional hemodynamic and mechanical data such as Wall Shear Stress (WSS) and vessel wall properties. These approaches have the potential to identify ATAA patients that despite presenting normal aortic diameter may benefit from earlier treatment. Nevertheless, these tools are not widely implemented in clinical practices primarily due to high uncertainty on the numerical results, difficulties in reproducibility on patient-specific applications, high computational effort and the lack of randomized controlled trials to assess the efficacy of computational models.

Abstract ID 29

ON THE DEVELOPMENT OF A NEW VEHICLE SAFETY SYSTEM FOR A STANDARD AND NON-STANDARD SEATING CONFIGURATIONS

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Keywords: automotive safety, non-standard configuration, nanobag, human body model, polymer

Summary: New trend in the automotive industry towards future vehicles brings new challenges in the passive and active safety features. The new seating configurations in the autonomous cars are hand to hand connected with new, and more complex crash scenarios, where the standard vehicle restrain and safety systems can lose their benefits or decreases level of their functionality. In the standard vehicles, the three main directions of the impact are to be considered, namely frontal, rear and side impact. However, changing of the seat positions and seating configurations will result in the multidirectional loading, and for such complex collisions, the safety systems must be adopted. This paper describes process of development of a new safety system, called nanobag: two thin layer curtain folded under the roof of the vehicle. Such technology consists of an elastic wall, brackets, gas generator and controlling system. They are all folded under the roof and deployed under sensor activation (similarly to the standard airbag). The main innovative of this system is in the material used for the curtain. It is a linear low density polyethylene (LLDPE), standardly used in the packaging and cargo of the goods. The main benefits of this system lay in the low material cost and weight, simply maintenance and non-sensitivity for out-of-position, which is one of the main weakness of the traditional airbags. The paper firstly describes experimental material testing of LLDPE, where simple pulling test with the small specimens (quasi-static and dynamic loading to include strain rate behavior) and drop test with the cylindrical impactor were performed. Authors used these data to build a LLDPE material model for the Virtual Performance Solution (VPS) software. LLDPE material reports orthotropic behavior in the two main perpendicular directions (machine direction and transversal direction) and such behavior needs to be considered in the testing as well as in the modelling. The validated material model of the LLDPE foil was included in the crash scenarios to test its behavior and benefits in the passenger safety. The study here considered frontal crash scenarios in 30 km/h and 50 km/h respectively and compared the safety assessment of the nanobag to the standard airbag for various anthropometries of the occupants. Next step of the development was to test the nanobag system in the non-standard seating configurations that are tightly connected with the future autonomous vehicles. Here, authors analyzed two new seat positions, where four passengers are facing to each other, as is assumed in the autonomous vehicles. The results show a good potential of this innovative safety system in the automotive safety. However, it is still under development, but such a solution can be considered for the further safety development to support current technologies toward safer vehicles.

Abstract ID 30

GYROID VS STRUT-LIKE SCAFFOLDS FOR BONE REGENERATION: AN IN SILICO COMPARITIVE ANALYSIS OF HEALING IN LARGE BONE DEFECTS

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Keywords: mechanobiology, finite element model, agent based model, 3D-printed scaffold, tissue engineering, gyroid, TPMS

Summary: Large bone defect treatment remains a clinical challenge. 3D printed scaffolds might help to overcome this challenge to stimulate regeneration of large bone defects by providing biomechanical cues to guide bone healing (Werner et al., 2017). Different scaffold designs have been analyzed for their healing potential with porosity, pore size, architecture, etc. being influential to the healing outcome (Pobloth et al., 2018). Gyroid scaffold designs have been discussed as a promising concept for their high surface area to volume ratio to enhance cell adhesion (Yoo et al., 2014). However, their regeneration potential remains to be investigated. The aim was to investigate the general potential of gyroid scaffolds to support bone regeneration compared to strut-like scaffold concepts. To allow a parametric comparison, an in silico approach was chosen to investigate the bone regeneration process within gyroid and strut-like scaffolds. The in silico models combined finite element (FE) analysis, to determine the mechanical environment within the scaffolds, and agent-based models (ABM) to characterize biological processes taking place during bone regeneration. Previously, we could demonstrate that such models are able to explain bone regeneration within titanium scaffolds (Perier-Metz et al., 2020). Both, gyroid and strut-like scaffolds had the same overall geometry: 5mm height and 79% porosity. Scaffolds were virtually inserted into a computer model of a large bone defect in a rat femoral osteotomy model, replicating a previously described experimental setup (Wehner et al., 2010). Scaffold pores were initially filled with granulation tissue, while PCL material properties were assigned to the scaffold. Moreover, scaffold pores were assumed to be filled with bone graft material (Perier-Metz et al., 2020). The spatial distribution of the initial mechanical stimuli within the gyroid and strut-like scaffolds were considerably different, despite being under the same overall mechanical loading. Initially, most of the tissue volume within the strut-like scaffold was under mechanical stimuli beneficial for bone formation. The gyroid scaffold resulted in higher initial mechanical stimuli, with relatively large tissue volumes under mechanical signals beneficial for cartilage and fibrous tissue formation. In both scaffolds, bone was predicted to start forming from the top and bottom surfaces and formation slowly progressed towards the center region by intra-membranous ossification. The healing outcome, however, was considerably different between the two scaffolds: while in the strut-like scaffold bony bridging was observed, the gyroid scaffold resulted in void regions within the scaffold core. Our results show that computer model predictions of bone regeneration are influenced by scaffold structure. This is in accordance with experimental studies showing different healing outcomes for different scaffold designs. Computer model predictions showed distinct initial mechanical

environments within the scaffold pores in the gyroid versus the strut-like scaffold. In addition, the large curvatures of the gyroid scaffold slowed down the penetration of the cells resulting in slower healing dynamics and reduced bone formation. Future studies will investigate the effect of other scaffold designs and further validate computer models by comparison of model predictions with experimental data.

Abstract ID 31

A MULTISCALE FINITE ELEMENT MODEL OF THE ELECTRICAL PROPERTIES OF THYROID TISSUE

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Keywords: Electrical Impedance Spectroscopy, Finite Element Modelling, Multiscale Modelling, Thyroid Tissue Structure, Tissue Type Discrimination

Summary: Thyroidectomy is a surgical procedure which is associated with several complications that can occur due to unintended damage of the parathyroid glands. One of the possible tools that could guide clinicians during the surgery is a probe exploiting the Electrical Impedance Spectroscopy (EIS) technique. This has previously been used to differentiate between tissues in their healthy and pathological states, based on the effects of the cellular structure on the flow of alternating current at different frequencies. Bearing in mind the evident differences in the microstructure between thyroid and parathyroid tissue, it is anticipated this will considerably affect the respective tissue electrical properties, allowing their differentiation. A finite element-based multiscale model is proposed in order to gain a better understanding of the structure's characteristics' effect on the electrical properties of thyroid tissue and to suggest potential improvements to the thyroidectomy surgical technique. Due to the capacitive nature of cellular membrane, biological structures exhibit a frequency-dependent decrease in impedance occurring around the kHz-MHz region. To overcome the computational resources limitations arising for the need to include these small structures, a multiscale modelling approach is implemented to study the electrical behaviour of thyroid tissue where three levels of complexity can be distinguished: i) thyrocyte (cellular scale), ii) follicle and iii) tissue scale level, the latter representing in vivo EIS measurements with a tetrapolar EIS probe. The lower-level real transfer impedance results are assigned to a higher-level model in the form of material properties calculated for each frequency. Several input parameters, comprising geometrical variability, different organisation of the structures and material properties uncertainties, have been investigated and the outcomes compared to clinical data. The computational modelling framework was created using Ansys® Mechanical APDL with quasistatic time-harmonic electric simulation. Of the geometrical parameters of the thyroid tissue structure studied, the sizes of the thyrocytes and follicles have the most significant impact on the impedance at frequencies below 10kHz, as well as on the shape of the dispersion. The best agreement between the theoretical and measured spectra has been observed for models with follicle size in the range 100-150 μm. Additionally, comparing the structured and random arrangement of follicles indicates that the organisation of these structures in thyroid tissue has a little effect on the resultant impedance, if the volumetric ratio of the model compartments is kept constant. The proposed modelling pipeline will be adjusted to the requirements of parathyroid tissue which exhibits more compact cellular structure compared to the thyroid gland. The ultimate aim is to identify differences in the theoretical EIS spectra, in order to support the clinicians in the EIS guided thyroidectomy procedure.

Abstract ID 32

BIOINSPIRED DENTAL IMPLANT CONCEPT, A FINITE ELEMENT STUDY

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Keywords: Bioinspired, finite element model, simulation, dental implants

Summary: Dental implants have emerged in society as a highly successful solution replacing missing teeth, although there are still reports of failure (Moraschini, et al. 2015). Thus, a bioinspired dental implant (BDI) has been developed and studied to reduce the rigidity of conventional dental implants and to promote a load transfer equivalent to that of a tooth. This study tried to evaluate the new dental implant concept behavior in comparison with the tooth. A tooth model in the mandible was developed. The periodontal ligament was considered to be a positive copy of the tooth root with a thickness of 0.2 mm (Tsouknidas, et al. 2016). The implant was inserted in the same position of the mandible, and a total osseointegration situation has been simulated. A convergence study has evaluated the mesh quality. Bidimensional and tridimensional simulations were performed. Compression tests to simulate the bite force were executed with a 100 N load and 30 degrees of inclination (Robinson, et al. 2019). Analyzing the results, BDI generated higher stresses in the facial side of the bone. This occurrence was not observed in the tooth model, which exhibited similar stresses in the facial and lingual sides. The BDI presented the capacity to reduce the strain and the stress in the proximal zone of the trabecular bone, exhibiting the higher values approximately at the middle of the implant length. Regarding the von Mises stresses registered in the cortical bone for the BDI, they were higher than the ones registered in the tooth model, although it will be interesting to compare the results in cortical bone with other commercially available dental implants. The bone quality also affects the stresses in the bone. For the trabecular bone, the stresses decreased with the decrease of the bone density, but the opposite occurred in the cortical bone. the bone growth inside the slits of the BDI, which is expected over time, has also been simulated. It was possible to observe that the model's displacement decreased with the increase of bone ingrowth, increasing the stability of the implant. Within the limitations of the simulations performed, since isotropic, homogeneous, and linear materials were considered, it was possible to observe the behavior of the BDI is similar to the tooth and can be an interesting solution with bone integration. In the future step, the model will be improved to consider the bone compression during implantation.

Abstract ID 33

MECHANICAL PROPERTIES OF BONE TISSUE ENGINEERING BIOCERAMIC SCAFFOLDS ASSESSED THROUGH MICRO-CT BASED FINITE ELEMENT MODELS

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Keywords: Bone Tissue Engineering scaffolds, computational models, micro-CT based models, glass-ceramic, hydroxyapatite

Summary: Assessing the mechanical properties of bone substitutes is of paramount importance in load-bearing applications. Glass-ceramics and hydroxyapatite are broadly recognized as suitable materials for Bone Tissue Engineering (BTE) thanks to their biocompatibility and bioactivity. However, the mechanical properties in the early stage after implantation may be not adequate, being affected by the intrinsic brittle nature of the constituent material as well as by defects induced by the manufacturing process and inadequate design of scaffold micro-architecture. In this study, two kinds of bioceramic scaffolds produced by additive manufacturing technologies are considered: glass-ceramic scaffolds obtained through the robocasting technique and hydroxyapatite scaffolds obtained through stereolithography. Specifically, the former exhibits a fiber distribution along with two perpendicular directions on parallel layers with a 90° tilting angle between two adjacent layers, whereas the latter closely replicates the architecture of a polyurethane foam used as virtual model. The mechanical properties of both scaffolds have been obtained through micro-Computed Tomography (micro-CT) based Finite Element Modeling. The micro-CT scans for the two classes of scaffolds have a pixel size of 5 μm and 10.5 μm, respectively; these spatial resolutions allow for the identification of micro-cracks induced by the sintering process as well as the deviation of the final geometry from the original design of the microstructure induced by the temperature treatment after printing. Elastic properties were assessed by applying 6 different unit macroscopic strains (one for each strain component) on a Representative Volume Element (RVE). As voxel-type finite element grids were used, each pixel was corresponding to one cubic finite element. The full elastic tensor is obtained thus providing elastic properties along any direction in the three-dimensional (3D) space. The strength was obtained through a damage-based cyclic algorithm. The non-symmetric tension/compression strength mismatch was assumed through a Drucker-Prager criterion. The constitutive parameters for the glass-ceramic and hydroxyapatite were assessed through micro-mechanical laboratory tests. In particular, elastic modulus was assessed through nanoindentation tests on glass-ceramics, while nanoindentation and micro-bending tests were used for hydroxyapatite samples. The micromechanical bending tests were performed on a set of samples exhibiting a characteristic size similar

to that of the trabecular microstructures of the 3D-printed scaffolds manufactured through the same printing technique (stereolithography). The obtained results have shown that the robocasted glass-ceramic scaffold exhibited an elastic modulus and strength which were weakly affected by initial fractures and small defects, while larger defects due to imperfect connections between perpendicular fibers affected the mechanical properties more substantially, especially along the direction perpendicular to the printing plane with an elastic modulus up to one-tenth of that of scaffold without this kind of defect. The HAp scaffolds exhibited an elastic modulus about one-tenth that of the bulk material, and quadratic dependency with the porosity. The uniaxial compressive stress-strain behaviour shows the typical trend of a foam-like structure, showing a compressive strength of 3% respect to the bulk material's tensile strength.

Abstract ID 36

FLUID FLOW OF BIOMIMETIC FLUIDS IN COMPLEX MICROCHANNELS FOR MICROCIRCULATION STUDIES

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Keywords: Blood analogue fluid, fluid characterization, surfactant concentration, microcirculation, microfluidics

Summary: Biomicrofluidics addresses as a common practice to use in vitro blood to investigate blood flow phenomena observed in real microvessels, However, this approach is not straightforward, as handling with real blood brings numerous difficulties related to sanitary, bureaucratic and technical problems. In this context, the use of biomimetic fluids flowing in microchannels has been explored within the last years, but in most studies, researchers still struggle with the properties of the blood analogues, particularly when mimicking red blood cells mechanical properties and flow behaviour. In this context, and following our previous work, the present study explores the use of a simple, stable and low cost 2-phase blood analogue fluid, which can mimic multiphase phenomena of real flow in microcirculation. The analogue fluid is compared with real blood, regarding its physical properties and the flow behaviour for complex PDMS - Polydimethylsiloxan microchannels, made using soft lithography. The microchannels geometry addresses bifurcations. The results on the particle size distribution confirm the reproducibility of the fluid preparation, as well as of its stability. The analogue fluid density is close to that of water, thus approaching the blood density. Furthermore, the blood analogue fluid depicts a shear thinning behaviour, matching that of blood, except for very high concentrations of surfactant. Fluid flow experiments show that the blood analogue can generate cell-free layers (CFL), with thickness close to that of real blood. Increasing the surfactant concentration promotes the augmentation of the CFL's, but also endorses agglomeration and clogging. Flow separation occurs also at the highest surfactant concentrations, which makes more difficult for the particles to follow the flow, so that flow field evaluation becomes more difficult.

Abstract ID 38

PERFORMANCE COMPARISON OF DEEP LEARNING SEGMENTATION MODELS ON HISTOLOGICAL SECTIONS IN A MURINE BONE ADAPTATION AND REGENERATION MODEL

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Keywords: deep learning, histology, bone, animal model, mouse, micro-CT, segmentation, multi-modal, UNet, Linknet, pre-clinical model, correlative imaging, Python, image processing, image analysis, machine learning, neural network

Summary: Histological analysis of bone samples from pre-clinical animal experiments is a well-established technique to investigate multiscale processes between tissue and cellular structures. Sections are stained for several bone metabolic and structural markers, such as Sclerostin and Safranin-O, supporting bone adaptation and regeneration studies. Nonetheless, the post-processing analysis is predominantly manual, limiting its throughput and integration into correlative multi-modal approaches that require segmented images to be registered to 3D micro-computed tomography (micro-CT) volumes of the same sample. Therefore, this work aimed to explore Deep Learning (DL) segmentation models to expedite the analysis of histological images of murine bone. A ground truth dataset of six Safranin-O and two Sclerostin stained histological sections (10µm thickness, with Fast Green counterstain) of a mouse femur was manually segmented using QuPath by two operators. All images were from the same mouse, obtained from a previous femur defect loading study [1]. Since only approximately 10% of the image pixels represented mineralised bone, a custom sampling algorithm was developed to generate a balanced training dataset. A total of 8640 patches (256x256) were extracted and zero-padded by 32 pixels. The Python package "segmentation-models" was used to compare four architectures (UNet, Linknet, PSPNet and FPN) and 35 backbones pre-trained on the ImageNet dataset. Four loss functions (Dice, Jaccard, binary focal and binary cross-entropy or binary CE) were available, and two evaluation metrics (intersection over union or IoU and F-score) were used for performance assessment. Linknet was selected to compare all backbones, given its speed and low resource usage, revealing a subset of the 12 best-performing options. Next, a robust loss function was determined by testing linear combinations of the four options available. A combination of Jaccard and binary CE achieved the most consistent results. Afterwards, a hyperparameter optimisation was performed on all architectures, combined with the 12 selected backbones and optimal loss function. A learning rate of 0.001, batch size of 16 and 200 steps per epoch were found to work best. An EarlyStopper callback was used to stop training when the loss function value remained constant for three consecutive epochs. UNet and Linknet were the best performing models, combined with seresnet101 and seresnet152 backbones, respectively, achieving an IoU score of 0.964 and 0.961. Furthermore, a model trained on Safranin-O images successfully segmented Sclerostin images, paving ways to transfer models trained on one type of marker to similar images. Overall, these results indicate that Deep Learning models can segment histological images from murine bone samples. Ongoing work will expand the models' performance assessment and the dataset's diversity to include

images with other relevant bone markers. This segmentation model will enable a higher throughput of a correlative multi-modal approach under development that combines *in vivo* micro-CT , *ex vivo* histological sections, and spatial transcriptomics data. We believe this Local *in vivo* Environment (LivE) imaging approach will reveal novel multiscale mechanobiological pathways regulating bone adaptation and regeneration and advance our understanding of the causes of unbalanced bone mechanoregulation, with a particular focus on ageing, and potential ways to improve it.

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Abstract ID 40

IMPLEMENTATION OF A MICROSOFT HOLOLENS 2 FOR SUPPORTING DIAGNOSIS AND MONITORING TREATMENT OF SCOLIOSIS

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Keywords: Scoliosis, Augmented Reality, Microsoft HoloLens 2, Diagnosis, Treatment Monitoring

Summary: Scoliosis is a condition in which the spine deforms to the left or right side, evaluated by a lateral curvature larger than 10 degrees. When observed from frontal view, the scoliotic spine may seem to be S-shaped or C-shaped. Idiopathic scoliosis is a complex 3D musculoskeletal deformity of the spine, developed by unknown reasons, that may seriously affect the patients' health, physical appearance, and quality of life. In younger subjects, aged 8 to 12, progression of the deformity status is more likely than in patients with finished skeletal growth. Several diagnostic methods, such as X-ray assessment, are employed if an anomaly is suspected and/or discovered. The Cobb angle, which is produced by two perpendicular lines drawn from the upper endplate of the topmost vertebra to the lower endplate of the lowermost vertebra from the most significant curvature segment, can be used to determine the severity of the curvature. Because of the growing deterioration of the spine, untreated scoliosis can lead to back pain and further complications in maturity. To make an appropriate assessment of the development deformity, radiographic images are required to evaluate and monitor the condition. Although radiography examinations cause a modest risk of radiation exposure, frequent examinations are linked to higher cumulative radiation exposure, which can have unfavourable repercussions for the patients' health. Because the tissues of growing youngsters can be particularly affected by x-ray radiation, radiography investigation should be reduced to a minimum. Based on earlier experimental results we made a hardware upgrade and used Microsoft HoloLens 2 as an Augmented Reality HMD to construct the cutting-edge application for aiding medical specialists in recognizing, recording, and tracking the evolution of adolescent idiopathic scoliosis (AIS). The application running on the Microsoft HoloLens 2 was designed with Unity3D, a programming tool for a range of platforms. The developed framework, designed in Unity3D, was primarily used to evaluate/assess and document the scoliosis condition. The basic function of the developed application is to identify the spinal curvature by using HoloLens's tracking system on the patients' dorsal surface, thus creating its 3D digital representation as a 3D mesh and allowing calculation of deformity curvature. In the following step, markers are placed on the prominent anatomical landmarks of the 3D surface using specially developed algorithms. A generic 3D model of a physiologically normal spine will be then registered with the patient-specific 3D surface. The application is able to display X-ray images taken for the same patients in accordance to the standard

medical practice. Other features include a data management system which enables archiving, searching and retrieving patients' medical records including 3D visualizations of the patient-specific spines. Another feature facilitates statistical analysis of the diagnostic parameters from follow-up monitoring sessions. Future application development will include a clinical evaluation by medical specialists which will be the backbone of the final ready to use solution in clinicals environment. This may include more sophisticated hardware like high-quality 3D scanners to improve the scanning process, generating the 3D model and enabling a dynamic spinal analysis.

Abstract ID 41

NUMERICAL EVALUATION OF THE PERMEABILITY OF IMPLANT WITH POROUS STRUCTURE

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Keywords: Permeability, Computational fluid dynamics, Porous structures, Porosity.

Summary: In recent years, porous structures, like lattices, have attracted the attention of researchers and engineers to develop new biomedical applications based in bioinspired designs. It is intended to overcome some of drawbacks of conventional applications, mainly in relation to their high stiffness and strength and poor biological response at the interface with consequent loss of osteointegration [1-4]. Scaffolds and in particular, implants with an outer layer with a porous structure would permit the supply of oxygen and nutrients, promoting bone ingrowth [5,6], providing implant stability with long-term fixation and osseointegration. Porosity, pore size and interconnectivity are key important factors influencing the permeability of such structures. The advent of new additive manufacturing technologies, deleveraged the production of such complex designs, with metal alloys. For this study, it was considered three implant layers with different porous structures (Geo_1; Geo_2; Geo_3). Geo_1 is based in diamond cell, Geo_2 is based in cubic cell and Geo_3 is based is hexahedral cell. The implants had 10 mm height and an outer diameter of 6 mm. The porosity was, respectively, 68%, 61% and 80% and pore size were, respectively, 270 mm, 440 mm and 290 mm. Within this study, it was performed a computational fluid dynamic (CFD) evaluation, to determine the permeability of the three different geometries, according to different studies reported in literature [7-9]. The numerical simulation was carried out in ANSYS® Fluent version 2020 R2 and the permeability was determined by measuring the pressure drop between the model ends and the volumetric flow rate through the porous structure, according to Darcy's law and takin into account that the Reynolds number was kept close to 1. For this study, liquid water was considered as "fluid" with density of $1e^{-3}$ g/mm^3 and viscosity of $1.01e^{-9}$ MPa.s. For the boundary conditions were considered a vertical velocity inlet of 1 mm/s [7], an outlet pressure of zero Pa and a no slip wall condition. In order to reduce computational time and cost, only one quarter of the model was considered and a symmetry condition was imposed. For the simulation, only the fluid part was considered. It was obtained the permeability values of $1.38e^{-9}$ m^2, $5{,}77e^{-9}$ m^2 and $1{,}83e^{-9}$ m^2 for Geo_1, Geo_2 and Geo_3, respectively. The obtained results revealed the importance of the geometry of structures to improve the permeability. Another important aspect is the pore size, because independently of geometry the pore size plays an important role and helps to increase the permeability. All the presented results showed that the permeability of all porous structures were in the range of permeability of trabecular bone, according to [7,10].

Abstract ID 42

NUMERICAL IMPLEMENTATION OF THE POLYLACTIC ACID (PLA) BEHAVIOUR DURING IMPLANT DEGRADATION

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Keywords: Polylactic acid (PLA), Degradation, Constitutive model, Hyper-elastic material, Finite Element Analysis

Summary: Polymers are widely employed in biomedical applications, like scaffolds for tissue engineering, stents, implants or in drug delivery systems, among others [1,2]. Polymers undergo an erosion or degradation process due to scission of their long molecular chains caused by hydrolytic reactions [3,4]. In particular, polylactic acid (PLA), is a biopolymer with good biocompatibility, biodegradability, good mechanical strength and process ability, being its biodegradation products the lactic acid (LA), which is biologically inert to growing cells [2,4,5]. In some cases, the degradation products can accumulate inside the polymer, mainly due to diffusion difficulties, leading to a process that accelerates the hydrolysis of the polymer, what is called autocatalysis. Diffusion has a major role in polymers degradation process. When it can be considered that diffusion occurs instantaneously all over the entire specimen, it is said that hydrolysis occurs throughout the material and it is called homogeneous or bulk erosion and when diffusion is very slow compared to hydrolysis, it occurs at the surface of the specimen and it is called heterogeneous or surface erosion. Factors such as crystallinity, crystal morphology or even the microstructure can influence the degradation rate of polymers [2,5].The degradation experienced by PLA is considered a stochastic process, drive mainly by hydrolysis, although some authors include autocatalysis and mechanical stimulation in their degradation models [3,6]. In this way, degradation of PLA accounts for the dependency of its properties over time. Apart some experimental work has been carried out and measurements of mechanical properties have been done [5,7], for each degradation stage, and models of the mechanical behaviour have been deduced, still lacks a clear and well-established understanding about the evolution of mechanical properties over time, during degradation [8]. In this work, a hyper elastic constitutive model and time-dependent model, from literature, were implemented in a simple model (50mmx50mmx10mm) made of PLA. The numerical approach, regarding the material properties and time-dependent models, were implemented in Ansys® Parametric Design Language (APDL). It was observed the predicted non-linear behaviour of PLA, during degradation and the decay of mechanical properties, according to [5,8].

Abstract ID 43

COMPUTATIONAL METHODS TO SIMULATE SPROUTING ANGIOGENESIS – NUMERICAL ANALYSIS WITH EXPERIMENTAL VALIDATION

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Keywords: Vascular endothelial growth factor, Angiogenesis evaluation, Capillary network, CAM assay, RPIM method.

Summary: Sprouting angiogenesis is the formation of new blood vessels from pre-existent vasculature. This process is regulated by several biological factors, being the vascular endothelial growth factor (VEGF) the main pro-angiogenic one. Angiogenesis is a complex process and computational models permit to study this process in different scales and using less time-consuming, reproducible and cheaper methodologies. Accordingly, this study aimed to simulate the chemoattractant effect of VEGF in angiogenesis. In our model, angiogenesis was simulated in a 5x5 mm^2 square domain, using a regular nodal mesh with 2601 nodes. Therefore, the endothelial cells migrate according to a reaction-diffusion equation for VEGF and the Radial Point Interpolation Method was used to solve its governing equations. A chick chorioallantoic membrane (CAM) assay was used to model the branching process. To validate the computational model and to analyse its predictive capacity, the capillary network profile and the angiogenic response for different VEGF concentrations, released from a biomaterial, were analysed and compared with experimental results. The developed computational model could simulate the angiogenic process modulated by VEGF diffusion. In all the performed simulations, endothelial cells migrated accordingly to the chemotaxis effect. Regarding the capillary network morphology obtained *in silico* and *in vivo*, some parameters were compared - total branching number, total vessel length and branching angle - and similar results were obtained (p-value higher than 0.05). Moreover, the capillary network pattern was compared between the *in vivo* and the *in silico* methodologies using the difference between the total capillary volume fractions and a good agreement was obtained with values between 10% and 15%. To analyse the predictive capacity of our model, the angiogenic response for different VEGF concentrations was analysed. The obtained quantitative results were very similar between the two methodologies used. In both CAM assay and simulation, the treatments with VEGF increased the total vessel number [CAM assay: VEGF 50ng increased 37% (vs. control, $p < 0.01$) and VEGF 100ng increased 82% (vs. control, $p < 0.01$); Simulation: VEGF 50ng increased 25% (vs. control, $p < 0.01$) and VEGF 100ng increased 75% (vs. control, $p < 0.01$)]. The treatments with VEGF also increased the total vessel length in both methodologies used [CAM assay: VEGF 50ng increased 20% (vs. control, $p < 0.01$) and VEGF 100ng increased 36% (vs. control, $p < 0.01$); Simulation: VEGF 50ng increased 18%

(vs. control, $p < 0.01$) and VEGF 100ng increased 44% (vs. control, $p < 0.01$)]. Moreover, the capillary network profile obtained in these simulations showed similarities to the one obtained *in vivo*. In conclusion, the capillary network from an *in vivo* assay was simulated with realist structure and morphology. Moreover, for the angiogenesis quantitatively analyses, the numerical results agree with the experimental ones, allowing us to conclude that our model could mimic the angiogenesis response modulated by different VEGF concentrations.

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Abstract ID 44

STABILITY OF TWO INTERNAL FIXATION IMPLANTS IN THE TREATMENT OF FEMUR FRACTURES: EXPERIMENTAL AND FINITE ELEMENT ANALYSIS

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Keywords: Hip fractures; Finite element analysis; Experimental tests; DHS

Summary: The number of medical devices available to perform interventions for hip fractures is already relatively high. Some are appropriate for fractures at the femoral neck, while others seem to be specially developed to stabilize the intertrochanteric area. This study correlates the experimental and numerical results of a new Trochanteric Plate of Contention (TPC), which may improve the resistance to the cut-out failure of internal fixation devices, and the well-known Dynamic Hip Screw (DHS) system. Generally, it is well accepted that the DHS is the first option in the treatment of stable femur fractures, as well as it is considered the implant that any new design should be compared with. Hence, two Sawbones® synthetic femurs, produced using the fourth generation of composite bones, were fractured and, posteriorly, fixed with the two fixation implants, i.e., TPC and DHS. The experimental study compares the strains, stresses, and displacements on these implants under compression loads after surgical stabilization of a neck fracture. Still, numerical simulations of the experimental setups were also carried out. Electrical and optical sensors assured the data acquisitions. The experimental results showed that strain values are higher in the DHS than in the TPC device, particularly in the neighborhood of the cephalic screw, while numerical results show that the biomechanical behavior of TPC is promising.

Abstract ID 46

GEOMETRY OPTIMIZATION OF REGULAR SCAFFOLDS FOR BONE TISSUE ENGINEERING: A MECHANOBIOLOGICAL APPROACH

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Keywords: Computational mechanobiology, Optimization algorithm, Tissue engineering, Fracture healing

Summary: We propose a mechanobiology-based optimization algorithm to identify the best geometry that regular scaffolds must possess to maximize the formation of bone, thus shortening the healing time. The computational mechano-regulation model of Prendergast and Huiskes was utilized to analyze the scaffolds mechanobiological response. The scaffold domain is modelled as a biphasic poroelastic material and the biophysical stimulus triggering the tissue differentiation process is hypothesized to be a function of the octahedral shear strain and of the interstitial fluid flow. The poroelastic FEM model of scaffolds based on different unit cell geometries was developed and incorporated in a numerical optimization algorithm that iteratively perturbs the scaffold geometry until the optimal one is determined, i.e. the geometry that favors the formation of the largest amounts of bone for the specific load value acting on the scaffold. Namely, the following unit cell geometries were investigated and compared: hexahedron with elliptic and rectangular pores, truncated cuboctahedron, truncated cube, rhombicuboctahedron, rhombic dodecahedron, diamond, hexahedron with spherical pores and FDM-based unit cell. In all these scaffold models, the mesenchymal tissue occupying the scaffold pores was simulated and the biophysical stimulus acting within this tissue when a compression load is exerted on the top scaffold surface was computed. A Python script was generated for each of the above-mentioned geometries that allows parameterizing specific dimensions of the scaffold unit cell. For each hypothesized load value, the objective function was determined, i.e. the ratio between the volume of the elements of the mesenchymal tissue that are predicted to differentiate into mature bone and the volume of all the elements of the entire scaffold model. *Fmincon*, the optimization tool available in Matlab to determine a constrained minimum of a scalar function of several variables, was utilized in the scaffold optimization process. Interestingly, we found that the optimal scaffold geometry is a function of the load acting on it. For very high load values, the scaffold with hexahedral unit cell and elliptic-rectangular pores is preferable to the others. For lower load values, the truncated cube unit cell seems to perform better than the others do. Finally, for high-medium load values, the rhombic dodecahedron unit cell appears preferable. In a context dominated by the so-called Precision medicine, where the therapy becomes a patient-specific procedure, the proposed algorithm appears to be a very promising tool capable of designing smart scaffolds, i.e. scaffolds suited to stimulate the formation of the largest amounts of bone on the specific patient with specific anthropometric features.

The algorithm can conveniently support the surgeon in the choice of the best scaffold geometry to be implanted on the patient, that is more capable to bear the load and to transfer it to the adjacent tissues, thus shortening the hospitalization and, in general, the healing times.

Abstract ID 47

COMPLEX BIOMECHANICS: EMERGENT PATTERNS FROM ATOMS TO PATIENTS

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Keywords: complex biomechanics, atom-to-beam homogenization, hereditary epidemiology

Summary: Complex systems are characterized by an overall behavior which is different from that of the components making up the systems - hence, (nonlinear) interactions between the components play a very important role. Taking an interdisciplinary approach rooted in theoretical and applied mechanics and engineering mechanics, we report on two types of recently studied systems where individual system components (atoms and patients) interact in a way which unfolds very interesting emerging patterns which can be mathematically quantified through concepts arising from (bio-)mechanics: (i) the interaction of atoms within a short thread of DNA, which, as a compound, result in family of a highly nonlinear beam structures with varying, but always coupled torsion-stretching modes [1]; (ii) the concession of sets of patients to the lethal effect of SARS-COV-2 [2], which was shown to follow integer-differential equations which were introduced by Boltzmann in the context of creep (or hereditary) mechanics. We conclude that smart classical concepts of applied mechanics and physics continue to show an unparalleled potential for solving pressing global problems in the context of computational bioengineering.

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Abstract ID 48

BIOMECHANICAL RESPONSE OF THE LUMBOSACRAL REGION L4-S1 DURING STANDING, FLEXION, AND EXTENSION MOVEMENTS, CONSIDERING THE TRABECULAR/CORTICAL BONE RATIO IN THE VERTEBRAL BODY: A FINITE ELEMENT ANALYSIS

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Keywords: Finite Element Analysis, Biomechanics, Lumbosacral Region, Trabecular/Cortical bone ratio, Lumbar Vertebrae

Summary: The arrangement of cortical and trabecular bone in the vertebrae is critical in the distribution of forces throughout the neuroaxis. The objective of this study was to quantify the biomechanical response of the L4-S1 vertebrae by a finite element analysis (FEA). A healthy lumbosacral spine (L4-S1) model was built based on a computed tomography through an assisted design program CAD - Materialise (Belgium). The anatomic structures included in the model were the main components of the vertebrae, the facet joints (FJ) with cartilage, the ligaments, and the intervertebral disk. The novelty of this study is the explicit presence of the trabecular/cortical bone ratio (TCBM) in all the components of each vertebra. The TCBM was compared with a solid cortical bone model (SCBM). We simulated a perpendicular force applied over the upper terminal plate of the L4 vertebra of 300N, 460N and 600N, in neutral and flexion-extension moments of 5 Nm and 7.5 Nm. Both models were solved by means of FEA in Mechanical Ansys Workbench (USA). Total deformation, maximum principal stress (MPS), von-Mises stress (VM), and maximum principal strain were the main studied variables. Regarding the pars interarticularis (PI), the TCBM had greater values in all postures compared to SCBM (27,5-40,46 MPa MPS and 21,14-42,28 MPa VM vs 14,83-32,16 MPa MPS and 7,19-11,38 MPa VM L5 neutral position). The FJ also had greater values in the SCBM compared to the TCBM, with lowest values in extension moment at 7,5 Nm (2,91-5,10 MPa MPS and 2,86-3,82 MPa VM vs 1,90-2,31 MPa MPS and 2,84-4,07 MPa VM in L5S1). In both models, the structure with highest stress values was the bilateral PI, followed by the FJ. This study evidence the importance of consider the trabecular/cortical bone ratio to perform computational simulations that are representative of the biomechanical behavior of the spine. The authors acknowledge the necessity of clinical validation of the model.

Abstract ID 52

THE ROLE OF INTRINSIC AND EXTRINSIC MECHANICS ON ENDOTHELIAL CELLS AND FIBROBLASTS ORGANIZATION DURING EARLY BONE HEALING: AN IN SILICO STUDY

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Keywords: computational mechanobiology, bone fracture healing

Summary: The initial phase of bone healing is a critical window for the ultimate healing outcome. During this phase, fibroblasts (FBs) and endothelial cells (ECs) are known to invade the healing region and self-organize reaching complex patterns. In vitro observations suggest the existence of a complex mechanical interplay between ECs and FBs through cells internally generated traction forces which in turn influence collective FBs organization and ECs sprout patterning; however, the details of this interaction in early healing remain largely unknown since mechanical signals are very dynamic and challenging to measure or investigate experimentally. Moreover, the mechanical environment within the fracture is substantially influenced by the external loading and the fracture fixation chosen. The aim of this in silico study is to investigate the individual and collective contribution of intrinsic and extrinsic mechanical cues on ECs and FBs organization during the early stages of bone healing. Exemplarily, a mouse model of fracture healing was selected and an in silico model of FBs and ECs organization within the healing region of an osteotomy stabilized with a rigid vs. semi-rigid fixator developed. Finite Element Models, to compute mechanical signals within the healing region, were coupled to Agent-Based Models, describing ECs and FBs activity [Checa et al., Ann Biomed Eng., 2009][Checa et al., Biomech Model Mechanobiol., 2015]. A feedback loop was implemented to account for the specific responses of ECs and FBs to local mechanical signals (e.g. durotaxis) and also include the effects of cell traction forces on the local matrix deformation. The iterative nature of the model allowed to obtain results at discrete time points simulating the first week post-osteotomy. Predictions at day 7 were compared to dedicated ex vivo histological data. After model validation, the in silico analyses were used to explore the relevance of alterations in cell traction forces and mechano-responsiveness. Vessels fragments, consisting of multiple ECs, were predicted to gradually align towards the lateral direction (i.e. perpendicular to the bone long-axis) while approaching the osteotomy gap, as observed experimentally. Furthermore, the lack of vascularity within the gap observed for the semi-rigid fixator was mimicked by the in silico analyses and could be explained by high mechanical strains locally. FBs were less prone to invade the osteotomy gap with the semi-rigid fixation as compared to the rigid one. Moreover, FBs were predicted to orient along preferential directions, in agreement with the direction of collagen fibres experimentally observed at later healing stages. The computer model predicted an altered cellular organization after cell mechano-response removal, while the inhibition of cellular traction forces did not produce a visible change. To our knowledge, this is the first in silico study that analyses collective ECs and FBs organization during early bone healing and comprises both cell internally generated

traction forces and externally applied loads. Collectively, our results identified external loads as the main player driving early ECs and FBs organization, suggesting that initial mechanical stability determines early cell patterning. The knowledge gained in this work should enable to support the development of strategies to foster bone regeneration.

Abstract ID 53

A MULTISCALE MODEL INVESTIGATING THE ROLES OF MINEARLISED COLLAGEN FIBRILS AND THE EXTRA-FIBRILLAR MATRIX ON BONE BIOMECHANICS

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Keywords: bone biomechanics; mineralised collagen fibrils, extra-fibrillar matrix; multiscale model; finite element analysis; molecular dynamics

Summary: Bone is a naturally occurring composite material whose constituent phases are hierarchically organized to provide a highly optimized structure that exhibits high stiffness and excellent resistance to fracture. At the sub-tissue level, lamellar bone represents a fundamental structural unit of the tissue and it consists of mineralized collagen fibrils (MCFs) embedded within an extra-fibrillar matrix comprised of hydroxyapatite minerals distributed throughout a matrix of non-collagenous proteins. While both intra- and extra-fibrillar phases provide a critical contribution to tissue-level behaviour, the mechanical implications of their structural arrangement and in particular the relative distribution of HA minerals between both phases, remains poorly understood. This study presents a multiscale computational framework that uses both finite element analysis and steered molecular dynamics to investigate the role of the MCFs and extra-fibrillar phases on the mechanical properties of bone tissue. At the nano-scale, representative volume elements (RVEs) of both MCFs and the extra-fibrillar matrix were developed within a finite element framework, and a homogenisation strategy was used to determine the effective elastic properties of each phase. At the sub-micron level, a RVE of lamellar bone that accounted for newly reported patterns of mineral platelets encircling mineralised collagen fibrils was used to predict the effective response of lamellar bone tissue, with material properties established from the previous length scale. The results demonstrated that the overall mineral content in the tissue is the biggest contributor to the effective elastic properties of lamellar bone. While this is perhaps unsurprising, importantly, it was demonstrated that the extra-fibrillar matrix (and mineral therein) is the phase that makes the primary contribution to the elastic response of the tissue. On the other hand, the predicted elastic properties of MCFs were much lower than the extra-fibrillar matrix, indicating that intra-fibrillar mineralisation only provided a modest contribution to the stiffness of bone tissue. To explore the role of MCFs in more detail, a steered molecular dynamics (SMD) framework was used to simulate tensile deformation until failure using LAMMPS software. A staggered MCF model was assumed, which had length and radius of 335 and 10nm, respectively. In this model, we considered mineral volume fractions of 5% and 35%, distributed in either intra-fibrillar or extra-fibrillar patterns. Interestingly, this study revealed that HA minerals themselves contribute to strain-hardening behaviour of MCFs, by resisting the characteristic sliding behaviour between adjacent collagen molecules. We also uncovered characteristic behaviour of mineralised collagen fibrils, whereby their tensile behaviour showed three distinct phases: (i) under initial elastic loading, the residual stress is released and shear loading between adjacent collagen takes place followed by (ii) sliding

of adjacent collagen molecules and (iii) work-hardening mediated by HA minerals until eventual failure by breaking the collagen molecules. In terms of failure, it was found that the Ultimate Tensile Strength (UTS) of the MCF reached its maximum amount as mineral become more uniformly distributed in the intra-extrafibrillar region, but this coincided with a reduction in elastic modulus of the MCF.

Abstract ID 56

A STUDY ON THE COMPUTATIONAL FLUID DYNAMICS AND FLUID STRUCTURE INTERACTION MODELS FOR THE HEMODYNAMIC OF ASCENDING THORACIC AORTA ANEURYSM

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Keywords: Ascending thoracic aorta aneurysm, Computational fluid dynamics, Fluid-structure interaction, Finite Element Method, hemodynamics

Summary: The ascending aorta is the first arterial segment that follows the left heart and is mechanically stressed by the blood flow that initiates the systemic circulation. Over time and due to changes in the microstructure of the vessel wall, the aorta may lose elasticity and dilate. If it increases by 50% over its original diameter in the ascending aorta, it is called an aneurysm. According to the European Society of Cardiology (ESC), this pathology should be diagnosed by measuring the diameter of the aorta. However, in practice, some patients have been observed to develop rupture or aortic dissection even before the criterion of minimum diameter has been reached. In this sense, it is generally accepted that the geometric diameter criterion must be assisted by other approaches that analyze multiple aspects to support the clinical medical diagnosis. Computational Fluid Dynamics (CFD) can provide a suitable tool, as it allows a real-time evaluation of the hemodynamic behaviour and is able to estimate future life-threatening situations, even after surgery, by geometry modification. To improve the reliability of the results, however, the CFD approach can be enhanced by considering the possibility to couple Fluid-Structure Interaction (FSI), thus incorporating the elastic properties of the structure and their effects on the hemodynamics to be evaluated in the numerical simulations. The present work aims to develop a methodology to perform a numerical study of CFD with FSI for the hemodynamic of ascending thoracic aorta aneurysm (ATAA). The geometric model and boundary conditions were extracted from Computed Tomography scan (CT) and 4D Magnetic Resonance Imaging (4D-MRI) imaging of the pilot patient. The open-source SimVascular software was used as a 3D segmentation tool, mesh generation, and numerical solver of Navier-Stokes equations and FSI. This methodology will improve the process of generating CFD numerical models to support the clinical outcome. In the future, this process will be automated to ensure consistent results.

Abstract ID 57

RAPID, PATIENT SPECIFIC OPTIMIZATION OF BONE SCAFFOLDS

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Keywords: Mathematical modeling, coupled systems of PDEs and ODEs, scaffold mediated bone regeneration, PDE constraint optimization

Summary: We first present a simple, efficient, three dimensional, time dependent model for bone regeneration in the presence of porous scaffolds to bridge critical size bone defects. The essential processes are an interplay between the mechanical and biological environment which we model by a coupled system of PDEs and ODEs. The mechanical environment is represented by a linear elastic equation and the biological environment through reaction-diffusion equations as well as logistic ODEs, modelling signaling molecules and cells/bone respectively. Material properties are incorporated using homogenized quantities not resolving any scaffold microstructure. This makes the model efficient in computations, thus suitable as a forward equation in optimization algorithms and opening up the possibility of patient specific scaffold design in the sense of precision medicine. The model can take into account patient specific parameter, for example the defect geometry or the rate of bone regeneration. Our numerical findings show that our model for example recovers and quantifies clinically relevant stress shielding effects that appear in vivo due to external fixation of the scaffold at the defect site. In the second part, we use this model as a PDE constraint for the optimization of polymer scaffold porosities. The result of the optimization procedure is a scaffold porosity distribution which maximizes a given objective function, e.g., the stiffness of the scaffold and regenerated bone system over the entire regeneration time, so that the propensity for mechanical failure is minimized.

Abstract ID 58

PIEZOELECTRIC-BASED INSOLE FOR GAIT ANALYSIS

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Keywords: Sensor insole, Instrumented insole, Piezoelectric sensors, Gait analysis

Summary: The activity of walking is one of the main movements performed by human beings, since this movement is indispensable for both mobility and personal independence. Thus, the act of walking becomes essential for the execution of most daily activities. In the last decades, two strands research lines have become the focus of attention by researches, resulting in an expressive number of works on the subject. The first with the development of techniques, studies and protocols that allow to understand, analyze, evaluate and characterize the gait behavior, and the second with the development of systems to obtain parameters related to gait, in order to facilitate its analysis and characterization, assisting researchers in the field of physical therapy in the study of gait. The identification of gait behavior, specifically the distribution of plantar pressure of the foot, both static and dynamic, allows applicability in areas such as: sports, health and assistive technology. In sports applications, for example, to analyze the gait behavior of high-performance athletes to apply protocols to improve training and prevent injuries. In healthcare applications, such as diagnoses of pathogens that have gait as one of the parameters for diagnosis and/or progression, such as Parkinson's disease or some dementias such as Alzheimer's. In assistive technology applications, to assess the gait of patients with spinal cord injury or patients with diabetes, specifically the pressure/force distribution of the plantar surface of the foot, can help measure the efforts exerted by the lower limbs of these patients, and it also becomes essential to provide subsidies for the adoption of effective strategies for rehabilitation. Thus, the present work presents the prototype of an insole made of polymeric material, easy to manufacture and low cost, instrumented with 4 commercial piezoelectric sensors (*MEAS 35005*) in pre-established positions that allow to obtain a mapping of the planar pressure of the foot and which can identify the 3 main types of steps (neutral, pronated and supine). Preliminary tests were carried out with this insole, under two different conditions: walking and foot dragging. The results obtained with these preliminary tests showed that it is possible to differentiate the behavior of the signal in the two conditions tested. Therefore, it is intended to improve this insole to use it as an instrument for obtaining parameters and gait characterization.

Abstract ID 59

TENSOR ELECTRICAL IMPEDANCE MYOGRAPHY OF THE TONGUE IN AMYOTROPHIC LATERAL SCLEROSIS IDENTIFIES THE IMPEDANCE SIGNATURE OF DISEASE PROGRESSION

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Keywords: Amyotrophic Lateral Sclerosis, Biomarker, Bioimpedance, Dimensionality Reduction, Electrical Impedance Myography, Linear Mixed Modelling, Non-negative tensor factorisation

Summary: Objectives: Electrical impedance myography (EIM) is a promising biomarker for amyotrophic lateral sclerosis (ALS). A key issue is how best to utilise high dimensional, multi-frequency data to fully characterise the progression of disease. Methods: Muscle volume conducted properties were obtained from EIM recordings across three electrode configurations and 14 frequencies and non-negative tensor factorisation (tensor EIM) was applied. Data were collected over a maximum of 9 months in 28 patients with ALS and 17 controls. Tensor EIM was evaluated against EMG data, the amyotrophic lateral sclerosis functional rating scale (ALSFRS) bulbar sub-score, tongue strength and an overall bulbar disease burden score. Results: EIM spectra with differing spectral shapes were seen in association with EMG findings of acute and chronic denervation. Tensor EIM identified both shapes in longitudinal measurements from patients with ALS, but with an increasing trend towards the spectral pattern associated with chronic denervation. Tensor EIM increased within three months ($p<0.01$) and continued to do so over the 9-month duration ($p<0.001$). In a hypothetical clinical trial scenario tensor EIM required fewer participants ($n=15$), than single frequency EIM measures (n range 28-189) or the ALSFRS bulbar subscore ($n=54$). Conclusions: Tensor EIM captures the effects of denervation/reinnervation and provides a sensitive measure of disease progression over time. Significance: There is currently a lack of objective biomarkers for the assessment of bulbar disease in ALS. Tensor EIM enhances the biomarker potential of EIM and can improve bulbar symptom monitoring in clinical trials.

Abstract ID 60

A MATHEMATICAL HOMOGENISATION APPROACH TO MASS TRANSPORT MODELS FOR ORGANOID CULTURE

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Keywords: organoid culture, multiscale, mathematical model, homogenization, transport, bioreactor

Summary: Organoids are three-dimensional multicellular tissue constructs used in applications such as drug testing and personalised medicine. We are working with the biotechnology company Cellesce, who develop bioprocessing systems for the expansion of organoids at scale. Part of their technology includes a bioreactor, in which organoids are embedded within a layer of hydrogel and a flow of culture media across the hydrogel is utilised to enhance nutrient delivery to, and facilitate waste removal from, the organoids. A complete understanding of the system requires spatial and temporal information regarding the relationship between flow and the resulting metabolite concentrations throughout the bioreactor. However, it is impractical to obtain these data empirically, as the highly-controlled environment of the bioreactor poses difficulties for online real-time monitoring of the system. Mathematical modelling can be used to improve the yield of organoids grown within the bioreactor, by predicting the metabolite concentrations during culture for different operating conditions. However, since millions of discrete organoids are grown simultaneously, modelling the mass transport and organoid growth is computationally infeasible in this multiply connected three-dimensional problem involving many moving boundaries of organoid-hydrogel interface. We present a general mathematical model for the transport of nutrient and waste metabolite to and from organoids growing within the hydrogel. We use an asymptotic (multiscale) approach to systematically determine the correct system of effective equations that govern the macroscale mass transport. We explore the homogenised model for different culture conditions for the bioreactor and show how these influence the hydrogel mass transport properties, highlighting the importance of the role of flow in the bioreactor in enhancing metabolite transport, and consequently improving organoid growth.

Abstract ID 61

TOWARDS FULLY AUTOMATED 3D RECONSTRUCTION OF HEART - SEGMENTATION AND PARAMETRIC HEART MODEL OF PATIENTS WITH CARDIOMYOPATHY

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Keywords: heart left ventricle, cardiomyopathy, machine learning, 3D reconstruction

Summary: Automatic diagnosis of dilated cardiomyopathy using cardiac ultrasound images is a complex process, as the primary challenges in developing an accurate and fast algorithm for automated left ventricle (LV) segmentation lie in the poor signal-to-noise ratio, weak echoes as well as the fact that pixel intensity levels in the images are not related to the physical properties of the tissue. This work focuses on the creation of an automated diagnostic tool based on (1) machine learning algorithms to segment region of interest, (2) geometrical algorithms to reconstruct 3-dimensional model of the heart and (3) finite element method to analyze the mechanical response of the left ventricle to different loading conditions. Dataset included 1809 images with an apical view and 53 images with an M-mode view from cardiomyopathy patients collected at three clinical facilities in the United Kingdom and Serbia. Methodology for apical view analysis included implementation of U-net convolutional neural network for LV segmentation which is followed by rectangle bounding box creation and extraction of longer side, which has a meaning of left ventricular length (LVL). The methodology was applied parallelly for both systole and diastole to extract LVLs and LVLd, respectively. For the M-mode view, due to smaller number of images, traditional algorithms such as adaptive histogram equalization, template matching, Canny edge detection and thresholding are applied in order to extract internal dimension (LVID), posterior wall thickness (LVPW) and interventricular septum thickness (IVS), both in systole and diastole at the same time in one image. When manually annotated LV and calculated related parameters are compared to the proposed methodology results, a dice coefficient of 92.091% for segmentation and an average root mean square error (RMSE) of 0.3052cm for parameter extraction in apical view images and an average RMSE of 1.3548cm for parameter extraction in M-mode view images are obtained. Based on calculated left ventricle length, radiuses, wall thicknesses, and user-supplied divisions, we build a 3D model of the left ventricle and we can use this model to simulate full cardiac cycle. The approach is now available on a user-friendly platform. Fully automated cardiomyopathy detection, 3D reconstruction and cardiac cycle simulation of the left ventricle using ultrasound images can help clinicians make faster decisions and establish reliable treatments.

Abstract ID 63

COMBINING EXPERIMENTS AND IN SILICO MODELING TO INFER THE ROLE OF ADHESION AND PROLIFERATION ON THE COLLECTIVE DYNAMICS OF CELLS

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Keywords: Surfaces, interfaces and thin films, Cell adhesion, Cell proliferation

Summary: The collective dynamics of cells on surfaces poses theoretical challenges with important applications in the study of morphogenesis, tissue engineering, and cancer [1]. Different mechanisms are at play, including cell-cell adhesion, cell motility, and proliferation. However, the relative importance of each is elusive [2]. We developed a particle-based model, which can be combined with experimental results to infer the rate of each mechanism [3]. *In vitro* experiments were performed using a culture of glioblastoma multiform (GBM) cell line, U87MG. The position of the cell nucleus was determined automatically with image processing algorithms and the time evolution of the spatial cell-cell correlation was analyzed over a period of 24 h. By parametrizing the adhesion and proliferation rates in the model, it was possible to reproduce the evolution of the two-dimensional spatial heterogeneous distribution of cells, which provides insight into the underlying dynamics. The results revealed a reduction in cell-cell adhesion in response to the increase of cell density in the substrate as a function of time. This mechanism is consistent with a reduction in contact inhibition and, consequently, an increase enhancement on cells' migration.

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Abstract ID 64

EFFECTS OF TENSION BAND IMPLANTS ON THE MECHANICAL LOADING OF THE FEMORAL GROWTH PLATE DURING GUIDED GROWTH IN ADOLESCENTS

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Keywords: FE-Model, Growth Plate, Guided Growth, Tension-Band Implant

Summary: Malalignment of the lower limb leads to permanent increased loading of one compartment in the knee joint, one of the most common causes of knee osteoarthritis. A preventive therapy is available for adolescents in the form of correcting the deformity through growth control by temporary hemiepiphysiodesis. Here one side of the growth plate is 'occluded' by a tension band implant. With this guided growth procedure, the malalignment can be corrected. In up to 50%, the leg deformity returns [1]: the so-called rebound effect. Both, the influence of mechanical loading on length growth of bones and the way how the loading of the growth plate is changed by inserting a tension band implant are poorly understood. The objective of the current study was to examine how the insertion of the implant changes the local stress and strain distributions in the growth plate. For the investigation of the mechanical situation, a non-individual 3D finite element (FE) model was created based on the data of 5 patients with valgus malalignment. Characteristic geometric parameters of the growth plate and femur were taken from preoperative 2D full-length standing X-ray images in the frontal plane. The knee joint contact forces at characteristic positions of the gait cycle were used as boundary conditions. The lateral and medial knee contact forces were determined through OpenSim based on the data of instrumented gait analyses [2]. For each chosen point of time and joint angle throughout the gait cycle, three FE models were built: one representing the state before treatment without implant, one immediately after implantation and one at the end of treatment when the implant itself is under stress due to bone growth [3].Results for standing on both legs show an inhomogeneous stress distribution in the pathological growth plate. As expected with valgus malposition, increased compressive stresses were observed laterally before insertion of the implant. The insertion of the implant initially reduces compressive stresses on the implant side, i.e. medially, but at the end of the treatment, higher compressive stresses occurred on the implant side medially and tensile stresses laterally. The shear stresses were also significantly higher and were now concentrated mainly on the implant side. Findings from the literature show that growth in the growth plate is inhibited by static compressive stresses and stimulated by tensile or shear stresses. These are the effects that occur due to the insertion of the

implant. The results will allow a better understanding of implant induced local changes in the mechanical loading in the growth plate and the resulting growth inhibition over the gait cycle.

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Abstract ID 65

MODELLING OF CELL-MEDIATED SELF-ASSEMBLED COLLOIDAL SCAFFOLDS

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Keywords: Self-assembly, Colloidal scaffold, Tissue engineering

Summary: A critical step in tissue engineering is the design and synthesis of 3D biocompatible matrices (scaffolds) to support and guide the proliferation of cells and tissue growth. Most existing techniques rely on the processing of scaffolds under controlled conditions and then implanting them *in vivo*, with questions related to biocompatibility and the implantation process that are still challenging. As an alternative, it was proposed to assemble the scaffolds *in loco* through the self-organization of colloidal particles mediated by cells. In this study, we combine experiments, particle-based simulations, and mean-field calculations to show that, in general, the size of the self-assembled scaffold scales with the cell-to-particle ratio. However, we found an optimal value of this ratio, for which the size of the scaffold is maximal when cell-cell adhesion is suppressed. These results suggest that the size and structure of the self-assembled scaffolds may be designed by tuning the adhesion between cells in the colloidal suspension [1,2,3].

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Abstract ID 66

AUTOMATIC CEPHALOMETRIC LANDMARKING OF CRANIOMAXILLOFACIAL COMPUTED TOMOGRAPHY SCANS USING A COARSE-TO-FINE DEEP LEARNING APPROACH

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Keywords: Deep Learning; Cephalometry; Orthognathic Surgery; Surgery, Computer-Assisted; Tomography, X-ray computed

Summary: Computer-aided orthognathic surgery planning must often deal with complex craniofacial deformities and would benefit from a standardized cephalometric analysis performed on three-dimensional (3D) craniomaxillofacial computed tomography (CT) scans. Such cephalometric analysis currently relies on manual localization of 3D landmarks on CT scans, requiring around 15 minutes for a trained and experienced clinician. In order to reduce the clinicians' burden, recent studies proposed deep learning-based models for automatic 3D cephalometric landmarking. The robustness and clinical usefulness of these results has still to be demonstrated, as most of these studies lacked a hold-out test dataset, localized a limited number of landmarks and/or did not clearly describe the database they used. The objective of this work was then to propose an automatic method for localization of multiple cephalometric landmarks on presurgical CT scans using a coarse-to-fine deep learning approach. High-resolution CT scans acquired before orthognathic surgery were randomly distributed among a training set (n = 128), a validation set (n = 32) and a test set (n = 38). The ground truth data consisted in 33 landmarks manually localized on each CT scan by trained and experienced operators: manual annotations of a single operator (n = 178) or means of the six annotations of three operators (n = 20, test set only). Six 3D Spatial Configuration Net networks were trained, either on full scans with a lowered resolution or on selected regions of interest (ROIs) with a full resolution. Inference was performed once on our test set following a 2-stage method. At stage 1, the full-scan network predicted the "coarse" localization of the landmarks, used to extract the 5 ROIs. At stage 2, the 5 other networks predicted the "fine" localization of the landmarks in the selected ROIs. To evaluate the overall localization performance of the proposed method, we computed mean radial errors (MRE) - Euclidian distance between the ground-truth and the predicted landmarks - and success detection rates (SDR) - proportion of landmarks located within a precision limit. Inference required around a minute per CT scan. On our test set, MRE for all landmarks was 1.14 mm (SD 2.09 mm) and SDRs for all landmarks were 89.64%, 92.85% and 94.62% using 2mm, 2.5mm and 3mm precision ranges, respectively. Eight landmarks (24.2%) showed an SDR at 2 mm of 100%; 22 landmarks (66.7%) showed an SDR at 2mm over 90%, and 5 landmarks (15.2%) showed an SDR at 2mm under 80%. These 5 least accurate landmarks are known to be the least reproducible in manual landmarking,

being localized on anatomical curves. Outliers over 10mm were found in a single CT scan, from a patient exhibiting a syndromic deformity (cleidocranial dysplasia).The proposed coarse-to-fine approach is a promising method for the automatization of cephalometric landmarking of craniomaxillofacial CT scans. Its evaluation on a challenging test set from clinical practice showed that most of the landmarks were localized within a limit of 2mm and that error-prone landmarks were the same for manual and automatic landmarking.

Abstract ID 67

INTEGRATION OF MECHANICAL STIMULI INTO AGENT-BASED SIMULATIONS OF INTERVERTEBRAL DISC CELL ACTIVITY

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Keywords: Intervertebral disc; Agent-based modelling; Network modelling; Mechanoregulation; Computational systems biology

Summary: Intervertebral disc (IVD) degeneration is a slow process, presumably affected by small persisting changes in cell activity (CA) that is assumed to be influenced by physiological activities. Microscale modelling can help to understand important processes that lead to micro injuries and therefore to tissue disorders over time. In previous work [1,2] we presented a 3D agent-based model representing Nucleus Pulposus (NP) cells within their mechanobiological microenvironment. CA was estimated based on experimental findings, integrated through parallel network methodology [2]. We addressed the effects of nutritional (glucose, pH) and inflammatory microenvironments, and hereby we tackle further coupling with key mechanical cues. Mechanical load magnitude (mag) and frequency (freq) were described as continuous, sigmoid-shaped functions, covering physiological ranges of mag (0.1-3.5MPa) and physiologically relevant ranges of freq (0Hz-40Hz). Functions were determined based on the literature (e.g. [3]). Normalized cell mRNA expressions were calculated for important mechanoregulated Extracellular Matrix proteins, i.e. Aggrecan, Collagen I and II, and the proteases MMP3 and ADAMTS4. Mathematical formulations were developed to approximate the sensitivity to chronic stimulus exposure, individual for each CA, based on experimental knowledge [4]. Eventually, the effect of load duration depended on the current load intensity and on the regulated protein considered. To evaluate the model, the effects of different physical activities (e.g. walking, sitting with active/round back, jogging) were simulated. Results predict sitting with an active back and walking as highly anabolic, whilst the anabolism of sitting with a round back and jogging was predicted to be highly time-sensitive. Thanks to the ability of this model to capture individual, time-sensitive responses of various mRNA expressions, the effect of different physical activities on NP cell responses could be observed for the first time. Findings were consistent with general expectations about the anabolic/catabolic cell stimulation induced by each physical activity. As a novelty, we could thereby show that cell responses were highly sensitive to the stimulus environment; whilst negative effects of jogging were related with a high activation of MMP3, sitting with a round back led to an activation of Col-I and ADAMTS4 mRNA expression, with minimal MMP3 alteration. Hence, the strength of this method is the possibility to compare physical activities by quantifying complex load combinations and considering loading duration, which aims to provide further insight in crucial factors contributing to tissue breakdown during normal life. This is the first IVD cell model, to our knowledge, able to integrate experimental findings, to estimate IVD cell activity within a mechanobiological, multifactorial environment.

Abstract ID 68

MECHANOTRANSDUCTION COMPUTATIONAL APPROACH OF CHONDROCYTES

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Keywords: mechanotransduction, osteoarthritis, protein-protein network modelling, dynamical systems, systems biology

Summary: Osteoarthritis (OA) is a debilitating joint disease, characterized by articular cartilage degradation, local inflammation, and pain. An extensive range of *in vivo* and *in vitro* studies provide evidence that mechanical loads induce changes in chondrocyte gene expression, through a process known as mechanotransduction (MT). MT involves cascades of complex molecular interactions that, when triggered, convert physical signs to cellular response(s) that favor chondroprotection or cartilage destruction regarding the nature of loads. Systematic representations of those interactions can positively inform early strategies for OA management, and dynamic modelling allows semi-quantitative representations of the steady states (SS) of the system according to imposed initial conditions. In cell biology, we would compare long-term cell activity or phenotypes to these SS or attractors. To this end, a novel network-based model (NBM) in the form of a continuous dynamical system of CC activity is proposed. The NBM incorporates key interactions from a corpus of 82 peer-reviewed articles from indexed journals. Then, an interactome is developed, consisting of a set of 115 nodes, i.e., cellular receptors, second messengers, transcription factors and proteins, related to each other through a specific topology of 256 directed edges. It is converted into a semi-quantitative mathematical model through a system of differential equations. To simulate a healthy SS of a CC including MT, the network is first stimulated with a physio-osmotic initial condition (TRPV4 and ($alpha_5beta_1$ activation). We further assess its capability to predict expected SS under inflammation and injurious loads (under static compression (ST) or high hydrostatic compression (HC) when PIEZO channels and patched receptor (PTCH) become activated). To validate the model, a qualitative validation (QV) is performed: we look for reported experiments and then we have counted how many of them can be replicated with our NBM. Results show that under physio-osmotic conditions, an anabolic SS is reached with low levels of matrix metalloproteinases (MMPs), and high levels of structural proteins. Pro-inflammatory and HC perturbations lead to a significantly different (t-test, a=0.05) CC expression profile, as a catabolic SS is reached, reflected by fully expressed pro-inflammatory cytokines and MMPs. ST does not have such a strong influence on chondrocyte metabolism, but it reduces the presence of anabolic indicators. Regarding transcription factors, healthy markers (Sox9 and CITED 2) are fully expressed under physio-osmotic conditions, and reduced under inflammation, HC and ST. Contrary, NF-kB and Runx2, characteristic of an osteoarthritic CC, are activated by inflammation, HC, and ST. Concerning the QV, our NBM can replicate 88% of the experiments tested, but PTCH related experiments could not be reproduced, suggesting the need for a targeted enrichment of the NBM.A regulatory network that maps intracellular signaling pathways of a CC was successfully developed. The model could predict expected MT and inflammation effects on general cell metabolism, revealing the potential of exploitation in OA.

Abstract ID 69

IN-SILICO TOOL FOR VIRTUAL HEMODYNAMICS OF FEMORO-POPLITEAL "BI-PASS" SURGERY

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Keywords: Peripheral arterial occlusive disease, Femoro-popliteal by-pass, Finite element analysis, FEA.

Summary: "Bypass" of the femoral-popliteal artery is indicated in the advanced stage of peripheral arterial occlusive disease. Surgical treatment is indicated based on clinical features, "ankle-arm index" and angiographic findings. In the finite element analysis method, a 3D model can be created based on scanning angiography, and various physical quantities can be measured to calculate the value of the "ankle-brachial blood pressure ratio". The aim is to depict arterial hemodynamics using the Finite Element Analysis (FEA) method, based on preoperative and postoperative scan angiography and physical parameters that can be measured in this way. This review presents "bypass" hemodynamics of the femoral-popliteal artery in preoperative and postoperative models. The model obtained from FEA shows pressure, shear stress, velocity, and streamlines. Pressure compared to values measured in the patient, "ankle arm index", preoperative and postoperative FEA results. Postoperatively, higher pressure and "ankle-arm index" values were measured in patients and models. The values shown in the model are significantly correlated with the values measured in the patient. Shear stress and velocity values are significantly reduced in the postoperative model. The streamline shows the predominant tibialis anterior artery. The physical quantity values measured in the patient and the model obtained by the FEM method correlate to a large extent.

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Abstract ID 70

SIMULATION OF THE FULL CARDIAC CYCLE USING PARAMETRIC LEFT VENTRICLE MODEL

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Keywords: Cardiac cycle, Holzapfel experimental model, Hunter muscle model, 3D parametric model

Summary: The study of processes in the LV is of primary interest. Heart dysfunction, diseases, and heart failure are often related to the tissue of the left ventricle. Numerical methods can give an insight into the mechanical response of the left ventricle under different conditions, before the execution of clinical trials and experiments. In our work, we generated a parametric model of the left ventricle with an aortic and mitral valve. During diastole, we prescribed inlet velocities to the mitral valve of the left ventricle, while velocity at the aortic valve is zero. During the isovolumetric contraction, both valves are closed, inlet and outlet velocities are zero, and muscles are activated by the prescribed calcium concentration function. To acquire passive stresses we used Holzapfel experimental material model and to acquire active stresses, produced in the muscle fibers, we used the Hunter material model. After the isovolumetric contraction, the aortic valve opens and the blood is ejected from the left ventricle through the aortic valve. Our numerical model can be used to simulate a full cardiac cycle with patient-specific data such as dimensions of the left ventricle and different velocities and calcium concentration functions, which can potentially help evaluate drug effects and clinical scenarios.

Abstract ID 71

NEW APPROACH TO STUDY SKIN VISCOELASTIC THROUGH SURFACE WAVE PROPAGATION, USING NON DESTRUCTIVE IN VIVO TESTING

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Keywords: viscoelasticity, surface wave, human skin, in vivo testing

Summary: Characterizing human skin using in vivo testing is quite a challenge. Traditionally, ex vivo tests are performed but as a living tissue, some information is lost. More recently, alternative methods were used for in vivo characterization. In our new method, we aim at characterizing skin with contact - less excitation and characterizing its rheology in vivo. To achieve that, we firstly investigate in vivo skin viscosity with a device developed at our laboratory; then we explore the surface wave propagation; and finally, we study the in vivo skin rheology through the wave propagation. First, we investigate in vivo skin rheology and, in particular, its viscosity. Traditionally on viscoelastic polymers, a creep recovery essay is carried out to characterize their rheology. We adapt this test to the skin for our approach: it is conducted on human skin with an applied constraint of 2.5 kPa during 300ms. As a result, we obtain a stress-strain curve. This curve is used to run an optimization routine that outputs the viscoelastic parameters of the tested sample. To describe creeping phenomena, we use a generalized Kelvin Voigt model, which is suitable to depict a creep response. Then, we explore the surface wave propagation. To successful observe the surface wave propagation, we use a harmonic solicitation. To carry out this test, we develop a device generating a blast od air impacting the skin. This blast is lasting 10ms and is equivalent to a harmonic solicitation of 100Hz. The stress, applied on the skin, is so brief that a surface wave is produced. We then measure this propagating surface wave. To compare a viscoelastic and a purely elastic material, we develop a numerical model to reproduce this test. Finally, this approach accesses the effect of the viscosity on the surface wave. Finally, we study the skin rheology using data extracted from the wave propagation. Inspired by geophysicists techniques, we compute a spectral analysis of the surface wave recorded. The analysis yields the main parameters of the wave propagation: phase velocities and attenuations. With these two parameters, it is possible to recreate the complex wavenumber of the surface wave, used after to compute the complex wavenumber of the shear wave. Then, we can express, thanks to the shear wave, the complex shear modulus and its complex viscoelastic moduli: the storage and the loss modulus. With these two, we write a fitting procedure to retrieve the viscoelastic parameters using any constitutive equation. To conclude, we create a new approach to characterize skin viscoelasticity. This approach is revealing the quasi - static behavior of the skin, using a creep - recovery test and its dynamic behavior, using surface wave analysis.

Abstract ID 72

AGENT-BASED MODEL AND SIMULATION OF ATHEROSCLEROTIC PLAQUE PROGRESSION

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Keywords: agent-based model, computer modeling, atherosclerosis, wall shear stress

Summary: Atherosclerosis is a local inflammatory disease characterized initially by the recruitment of leukocytes into the arterial wall. Arterial walls can develop plaques comprising of lipids, fatty substances, cholesterol, cellular waste products, elastin, fibrin, calcium and other constituents. The rate of production of these constituents are different in the disease progression stages. The described numerous components contribute to plaque creation and progression, each one with proper characteristics, behaviour and rulesets. The interaction between these components and the environment they evolve determines plaque progression. Agent-based modelling (ABM) is selected as a proper approach to reproduce the evolution of plaque progression and artery reshaping by simulating the behaviour of autonomous cellular agents (components). The dynamic system allows for complex phenomena to emerge from the interaction of simple rule-based behaviour of agents, living in a dynamically reshaping environment. We hypothesize that ABM model represents a reliable prediction model that is able to describe adequately history of atherosclerosis development. As a result, we created a multiscale atherosclerosis modeling framework based on ABM 2D modelling that simulates the hemodynamic-driven artery wall and plaque development. The model included behaviour of cells, Extracellular Matrix (ECM), and lipid dynamics in a variety of vessel cross-sections. A sensitivity study was also carried out to assess the oscillation of the ABM output in response to changes in the inputs and identify the ABM parameters that have the highest influence. The ABM results were mostly influenced by cell and ECM dynamics, which had a substantial impact on the lumen area. A group of factors was discovered that influence the ultimate lipid core size while having no effect on cell/ECM or lumen area trends. A full coupling of computational fluid dynamics (CFD) and agent-based modelling (ABM) framework would include simulation computed hemodynamics in a 3D artery model, coupled with ABM 2D modelling in order to characterize atherosclerotic morphological and compositional alterations in the arteries.

Abstract ID 73

NOVEL APPROACH IN DESIGNING MICROFLUIDIC DEVICES BASED ON FINITE ELEMENT AND TOPOLOGICAL OPTIMISATION METHODS

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Keywords: microfluidic devices, chip, FEA, topological optimization, in silico testing

Summary: Preclinical experiments require reliable, physiologically relevant systems that can reproduce complex human physiology. Further technological advances are urgently needed to gain a better understanding of the important biological processes, like circulation networks for the discovery and screening of new drugs. Traditional 2D and 3D in vitro approaches are widely used, but they cannot reproduce the complexity of native scenarios. These models are generally static and lack vasculature and shear stress forces, typically failing to reproduce the rheological properties of the physiological processes. Similarly, in vivo animal models rarely mimic human conditions, the results may not be fully representative of those obtained in humans, and they are ethically questionable. A new paradigm has emerged in preclinical modeling aimed at overcoming the limitations of previous methods. A combination of advanced tissue engineering, cell biology, and nanotechnology has developed a state-of-the-art microfluidic model with an unprecedented ability to reproduce the natural habitat of cells and tissues in microfluidic devices. The main issue with those devices is a consistent fluid distribution trues them. The construction of chambers and channels has a huge impact on the distribution of nutrients and drugs in each part of the device (to each testing tissue on a chip). This paper describes a novel approach in designing chip devices by using the finite element method (FEM) and topological optimization (TO) method for in silico testing and optimizing the shape of the features (chambers and channels). This approach minimizes mistakes in features design and provides the full potential of novel microfluidic devices.

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Abstract ID 74

ANALYSIS OF CARDIAC WORK AND SIMULATION OF AORTIC VALVE STENOSIS

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Keywords: Aortic valve stenosis, Finite element analysis, Computational simulation

Summary: The main aim of this work is to describe and analyze the basis of cardiac work and aortic root with stenosis, as well as to perform computational simulation of aortic stenosis employing patient-specific 3D analysis. In case of heart malformations, complex changes in left ventricular geometry are in most cases caused by continuous exposure to cardiovascular risk factors and/or hemodynamic conditions, which usually start as a physiological response. Cardiac work provides incremental information of left ventricle ejection fraction and strain which are sensitive to left ventricle afterload and related to non-invasive assessment of different types of cardiomyopathies. This is related to biomechanical alternations in case of aortic stenosis, a narrowing of the orifice of the aortic valve that causes an increased resistance to blood flow from the ventricle into the systemic circulation. Altered cardiac work, associated with aortic stenosis is commonly related with significant morbidity, mortality and healthcare costs. The presented study gives the insight into the model-based simulation of cardiac work and aortic stenosis, employing the in-house finite element PAK software and aims to propose an advanced approach for the assessment of work indices and biomechanical characteristics (stresses, pressures, displacements) based on computational modelling. PAK is a high-performance finite element (FE) software for solving complex coupled multi-physics/multi-scale problems, with main application in cardiovascular domain. It also can interact with different computational solutions and solvers. The computational modelling based on FE analysis could offer solutions to some of the problems in current healthcare practice, while its ability to run simulations and be predictive could help to identify the likely outcomes for patients. The performed study is the first step in further investigation and development of more advanced and complex 3D models.

Abstract ID 75

BIOREACTOR DIGITAL TWIN - AN ESSENTIAL MODELLING TOOL TO ESTIMATE LOCAL CELLULAR ENVIRONMENTAL CONDITIONS IN EXPERIMENTAL TISSUE ENGINEERING

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Keywords: Tissue Engineering Numerical Models, Bioreactor Models

Summary: Recent meta-research in tissue engineering points out that a lack of control on cellular environmental conditions persists in mammalian cell cultures [1]. Cell local environmental parameters like dO2, dCO2, temperature or pH, are many times assumed to remain constant and left unsupervised without any control during the experiment. Regarding cell stimulation using electromagnetic or mechanic forces (fluid flow, ultrasound, hydrostatic pressure), in recent studies [2, 3], our group found huge variability in the different stimulation parameters involved, e.g. magnitude, frequency, waveform, duty-cycle. Some of these parameters, such as the electric field magnitude, spread a range of more than 6 orders of magnitude when comparing different experimental protocols or their numerical model predictions. Despite these differences, these studies report similar biological effects on the cell culture, which remains a drawback. To surpass difficulties in cell monitoring and to improve the prediction of the cellular environment, we propose a numerical framework involving a digital twin model of a bioreactor to better guide researchers, when choosing the environmental conditions, and adjusting their hypothesis to the real bioreactor system. This framework will also contribute to avoiding protocol mistakes during the in vitro experiments and may help with the definition of the design, setting construction parameters (component sizes, channel dimensions, or input variables magnitude) allowing to reach the desired environment surrounding the region of interest for a particular type of cell. Future multi-scale models may fuse the current bioreactor and scaffold models with different cellular models. Integrating cellular dynamics like movement, growth, secretome, and eventually, tissue-like interactions or cell relations may open new doors for tissue engineering strategies. Additionally, with the currently existing models, just by continuously predicting and adapting the culture conditions to the cellular differentiation phase and cell population needs, it will be possible to accommodate cell development in an environment that closely mimics the in vivo conditions.

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Abstract ID 76

AUTOMATIC SEGMENTATION OF THE SPINE AND LOWER LIMBS BASED ON DEEP LEARNING IN LOW-DOSE BIPLANAR RADIOGRAPHS

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Keywords: Deep Learning, Segmentation, Low-dose X-ray, Biplanar radiographs, 3D Reconstruction, Spine, Lower limb

Summary: Three-dimensional subject-specific reconstruction of the spine and lower limbs based on low-dose biplanar X-rays is now available in clinical routine. These methods enable 3D visualization and quantification of 3D deformities such as scoliosis. Although the validity and reliability of these methods were already evaluated, these reconstructions require manual input and adjustments from well-trained operators. The reconstruction time is then significant, and therefore a hindrance for a large-scale use of such methods. Full automation is therefore of great interest. To that end, bone detection, classification and segmentation can be of tremendous value for replacing manual inputs. Segmentation methods exist for isolated bones, but a different framework is used for each bone. Therefore, we propose a single deep learning framework for joint detection, classification and segmentation of the spine and lower limbs. A database of 138 biplanar radiographs, with spine and lower limbs reconstructions, comprising of 20% of scoliotic patients was collected retrospectively. It was used to train and evaluate our method using a 5-fold cross validation. Ground truth segmentations of the spine, tibias and femurs were obtained by reprojection of the 3D models on the radiographs. The classification and segmentation was split into three separate steps through a coarse-to-fine approach. The first step consisted in the segmentation of the images at $1/4^{th}$ of the resolution. The obtained masks allowed an error-free calculation of bounding boxes for finer delineation of each structure. The second step consisted in the segmentation in the sagittal view of each lower limb with half resolution allowing the network to detect both femurs and tibias with better performance. Indeed, these segmentations were obtained with a mean Dice Similarity Coefficient (DSC) of 0.92 (mean SD = 0.07). The last step consisted of the segmentation of four subparts of the spine in full resolution: cervical, upper/lower thoracic and lumbar spine. At each step, we used nnU-net, a variant of the fully convolutional neural network U-net, which can automatically optimize hyperparameters. A mean DSC of 0.89 (mean SD = 0.06) and 0.92 (mean SD = 0.04) was obtained in the frontal and sagittal views respectively. To the best of our knowledge, this is the first automatic segmentation of both full spine (from C3 to L5) and lower limbs with a single framework. Our method obtained comparable results with the literature in a full body manner and can deal with severe scoliosis. The computational time for the prediction of the neural network was less than 10 seconds per image. From these segmentations, we can then gather structures and points such as the spinal midline

and joint centers that are needed in the 3D reconstruction process. In clinical routine, a trained operator currently manually digitizes these points. The proposed method has then the potential to replace the tedious manual inputs for the 3D reconstruction of the spine and the lower limbs. Moreover, some of these results can be used to compute simple 3D radiographic parameters, especially in the lower limbs (e.g. Hip-knee angle, hip-knee-shaft angle...), and could potentially be used in quick, timesaving posture analysis.

Abstract ID 77

EXPERIMENTAL AND COMPUTATIONAL FRAMEWORK TO DESIGN WELL-ORGANIZED FIBROUS SCAFFOLDS FOR CARDIAC TISSUE ENGINEERING

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Keywords: Biologic Ventricular Assistant Device, Finite Element Modeling, Myocardium mechanical characterization

Summary: Myocardium infarction (MI) provokes the necrosis of an area of cardiac muscular tissue. This results in a reduction of myocardium mechanical and electrical properties and a consequent loss of pumping capacity. One of the most standardized treatments is the application of a ventricular assistant device (VAD), though these devices do not constitute a long lasting solution. One recent promising approach consists on the development of a Biologic VAD (BioVAD) that can restore the myocardium pumping capacity. This device consists of a polycaprolactone (PCL) fibrous scaffold, printed by Melt Electrowritting (MEW), that is then filled with a cell laden hydrogel. In this work, we focused on the designing process of the BioVAD scaffold, aiming to optimize its mechanical response regarding the physiological requirements that will withstand once implanted. PCL hexagonal-shaped-fibrous scaffold samples were fabricated as previously described [1]. Their mechanical response was evaluated by uniaxial and biaxial testing, in order to guarantee an appropriate three-dimensional characterization at different loading scenarios. An elastoplastic constitutive material model was selected considering the obtained results for the preconditioned scaffolds. Great fit of our material model was observed at physiological strain range (15-25%). A parametric finite element computational model was created and validated. We also developed scaffold + hydrogel models to study the influence of the hydrogel on the global mechanical response. 5% GelMA hydrogel was considered, using an hyperelastic model with an overall stiffness of 5 kPa [2]. To study the mechanical influence that the BioVAD will have on the heart, we also performed an experimental characterization of myocardium tissue, aiming to understand the requirements that the BioVAD will have to satisfy at operating conditions. Biaxial and shear tests were performed into healthy and infarcted myocardium [3]. Scaffold + Hydrogel models obtained a significantly stiffer response, suggesting that the hydrogel may have a great impact on the global mechanical behaviour. The mechanical trials performed with cardiac tissue reflected an orthotropic behaviour respect to the muscular fiber direction, which agrees with the results observed at the literature [3,4]. A computational model of a BioVAD-specific PCL scaffold was created and validated, including scaffold + hydrogel models. Hydrogel consideration has proved to be essential for a proper mechanical design. We also performed an experimental characterization of cardiac tissue, obtaining a similar

response to the previous studies. With all this data, we are able to analyse the mechanical interaction between the BioVAD and the infarcted heart, which will allow us to improve the BioVAD design and to assure its success once implanted.

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Abstract ID 78

NUMERICAL SIMULATIONS OF STANDARD MECHANICAL TESTS FOR THE DEVELOPMENT AND OPTIMIZATION OF FULLY BIORESORBABLE STENTS

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Keywords: In vitro mechanical test, vascular scaffold, bioresorbable PLLA stent, design and optimization, finite element analysis

Summary: Standard mechanical tests are required according to ISO standards for stents produced for the purpose of deployment within coronary arteries. The development of a stent design that successfully passes all experimental tests is a time-consuming, difficult and expensive process, which consists of several stages and requires many cycles of mechanical testing and redesigning of the basic model. On the other hand, in-silico mechanical tests could reduce the cost and the number of necessary real mechanical tests. In this paper we use a recently introduced material model of poly-L-lactic acid (PLLA) fully bioresorbable vascular scaffold and recently empowered numerical InSilc platform, in order to perform in-silico mechanicals tests of different stent designs with different material and geometrical characteristics. In this work we compare and analyze the impact of strut thickness on mechanical characteristics of AB-BVS scaffold, as well as the impact of additional pocket holes (slots) in stent geometry on mechanical characteristics of Renuvia-PLLA stent. The numerical results and corresponding analysis are provided for each of the stent designs, and for four different tests: radial compression, inflation, three-point pending, two-plates crush resistance, local compression, kinking and flex.

Abstract ID 80

SILICOFCM PLATFORM, CARDIOMYOPATHY AND ELECTROMECHANICAL COUPLING

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Keywords: left ventricle, cardiomyopathy, electrophysiology, electromechanical coupling

Summary: We presented heart modeling using simulated drugs for cardiomyopathy and electromechanical coupling of the left ventricle and whole heart in the SILICOFCM project. The geometry of the heart with seven different regions of the model was included: 1) Sinoatrial node; 2) Atria; 3) Atrioventricular node; 4) His bundle; 5) Bundle fibers; 6) Purkinje fibers; 7) Ventricular myocardium. Monodomain model of modified FitzHugh-Nagumo model of the cardiac cell was used. Six electrodes (V1-V6) were positioned on the chest to model the precordial leads and the results were compared to real clinical measurements. Inverse ECG method was used to optimize potential on the heart. A whole heart electrical activity in the torso embedded environment, with spontaneous initiation of activation in the sinoatrial node, incorporating a specialized conduction system with heterogeneous action potential morphologies throughout the heart was described. Body surface potential maps in a healthy subject during progression of ventricular activation in nine sequences which were corresponding to ECG signal were presented. Finally, the results with parametric model and PV diagrams depending on the change of Ca2+, elasticity of the wall and the inlet and outlet velocity profile are presented. It is directly affected to the ejection fraction function. Future research will be more focused on in silico clinical trials where we will compare some clinical pathology findings on the body surface with standard 12 ECG electrode measurements.

Abstract ID 81

REALISTIC 3D PHOTO-RECONSTRUCTION FROM CBCT IMAGES

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Keywords: image fusion, CBCT, orthognathic surgery, 3D imaging

Summary: Orthognathic surgery is a surgical procedure that corrects the intermaxillary discrepancy, promoting a significant improvement in chewing and breathing, which contribute to the patient's well-being and psychological condition. During surgery planning, orthodontists often use two-dimensional imaging techniques. However, these techniques had some disadvantages compared to three-dimensional ones, namely non-detection of facial asymmetries and distortion of cephalometric points outside the medial sagittal plane. The evaluation based on CBCT images and dental cast models tries to overcome these limitations but soft tissue evaluation remains complex. Both orthodontists and maxillofacial surgeons make an effort to mentally merge the photographic and CBCT images to predict the outcome of the treatment. The objective of this work was to develop a co-registration method that would allow a realistic reconstruction from CBCT images. From the CBCT images, a three-dimensional rendering was performed followed by a segmentation of the soft tissues, allowing to obtain the cranial external surface. A co-registration between the obtained surface and a frontal photograph of the subject was then carried out. From this mapping, a photo-realistic model capable of replicating the features of the face was generated. To assess the quality of this procedure, orthodontists were asked to fill in a survey on the models obtained. The method developed was automatically applied to nine cases, and four were randomly chosen for the survey. The survey results show that orthodontists consider the three-dimensional model obtained to be of high quality and realistic. The method developed can automatically obtain a three-dimensional model from CBCT images allowing the visualization of the results of surgical-orthognathic planning.

Abstract ID 82

CLASSIFICATION OF CELL BIOMATERIAL INTERACTION TOXICITY LEVEL USING CONVOLUTIONAL NEURAL NETWORKS

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Keywords: cell, biomaterial, toxicity level, convolutional neural network

Summary: The medical image analysis field is highly dependent on good quality research time offering a noninvasive analysis and diagnosis of a medical problem. The most recent research credits the developments of different machine learning techniques for higher accuracy compared to traditional methods when analyzing more complex problems. Lots of research is being done towards the interactivity of the cells with different biomaterials, in order to provide an automatic model to determine the toxicity level. In this research, we will focus on different classification techniques using a convolutional neural network (CNN) of cells residing in different biomaterials. The problem is studied as multiclass classification: healthy, unhealthy, and severely disintegrated. The images are taken using a brightfield microscope, hence several image preprocessing techniques are applied to achieve high accuracy levels of predictions. The dataset used in this study includes approximately 20000 images for training and two different datasets with each more than 8000 images of size 128x128 pixels. LeNet architecture is used to analyze and classify the images. The network has four convolutional layers with kernels of size 5x5 applied, followed by max-pooling layers with the purpose of decreasing the number of weights. Without the preprocessing steps, the highest accuracy reached was 95%, whereas using several image preprocessing techniques increased the accuracy significantly. The highest resulting accuracy after preprocessing only the healthy part of the dataset with the Sobel filter was that of 99%.

Abstract ID 83

EFFECTS OF ELECTRICAL STIMULATION CONDITIONS ON HUMAN MESENCHYMAL STEM/STROMAL CELLS OSTEOGENIC DIFFERENTIATION: REFINING PROTOCOLS TOWARDS ENHANCED IN VITRO BONE FORMATION

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Keywords: Bone, Computer modelling, Electrical stimulation, Mesenchymal stem/stromal cells, Osteogenic differentiation

Summary: Endogenous electrical fields are known to drive key cellular processes such as cell proliferation, migration, differentiation and tissue development. Electrical stimulation (ES) has been described as a promising strategy for bone regeneration treatments in several clinical studies [1, 2]. However, the underlying mechanism by which ES augments bone formation is still poorly understood. Thus, this work aims to study the effects of five different ES protocols on the viability, proliferation and osteogenic differentiation of human bone marrow-derived mesenchymal stem/stromal cells (hBMSCs). For that, we started by developing an electro-bioreactor device (similar to the one described in [3]) based on a custom-made lid containing medical-grade stainless steel wire 316LVM electrodes and which was able to fit a standard 6-well tissue-culture treated polystyrene plate. The lid was fabricated by fused deposition modelling (FDM) using C8 material, which was proven non-cytotoxic in our previous work [4]. ES protocols based on electric potential (constant-DC or pulsed-AC) were performed using a power source equipment, while the protocol based on electric current application was done using a custom-made current pump electric circuit. The electrical fields delivered by the electro-bioreactor system to the cell cultures were predicted by computer modelling. More specifically, the impact of electrode size and positioning as well as of the culture medium volume on the distribution/magnitude of electrical fields was evaluated by conducting a Finite Element (FE) analysis using the AC/DC module of COMSOL Multiphysics. The different ES protocols (STIM 1 OM - 1.2V DC, 1 hour/day; STIM 2 OM - 1.2V DC, 1 sec/day; STIM 3 OM - 0.03 mA DC, 1 hour/day; STIM 4 OM - 1.2V AC, T=10 sec, 1 hour/day; and STIM 5 OM - 1.2V AC, T=2 sec, 1 hour/day) were applied every 2 days during 2 weeks while culturing the cells in osteogenic induction medium in an incubator at 37°C and 5% CO_2. Cells cultured in standard growth medium (BM CTRL) and osteogenic medium (OM CTRL) for 14 days without ES were used as controls. The *in vitro* experimental results showed that none of the different ES protocols impaired normal cell viability, morphology and metabolic activity. Moreover, the osteogenic differentiation of hBMSCs was supported by all ES protocols as confirmed

by the positive alkaline phosphatase (ALP)/Von Kossa stainings performed after 14 days of culture. The osteogenic differentiation of hBMSCs under the different ES protocols was also assessed quantitatively by the determination of ALP activity, calcium content and osteogenic marker genes expression (RT-qPCR analysis).In overall, this study highlights the advantages of using computer modelling in the definition and optimization of ES protocols for improved *in vitro* stem cell-based osteogenesis towards the development of novel tissue engineering strategies for bone regeneration.

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Abstract ID 85

PERDITION OF LOAD TRANSFER IN BIOINSPIRED CONCEPTS FOR BONE IMPLANT INTERFACE, A FINITE ELEMENT STUDY

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Keywords: Biodesign, Bioinspiration, implant interface, load transfer, Finite Element Analysis

Summary: The bone implant interface is critical for the implant integration and the load transfer between implant and bone. The orthopaedic registers presented in the main arthroplasties as hip and knee the aseptic loosening the most frequent failure in the prosthesis. Several studies suggesting implant coatings increasing the surface roughness or add hydroxyapatite and other bio-active interfaces to improve the bone osseointegration. The main objective of the present work is evaluating the load transfer in the bio-inspiration structures at the implant interface as interface concepts. Based in the nature, five interfaces of implant were designed to improve the bone implant osseointegration. The inspiration used for interface bio design was the trabecular bone structure, the bamboo structure, sea sponge, the gecko foot structure and spore of mushrooms. Each bio interface structure was designed to guarantee the same size of pores around 500?æm and the same thickness in the implant base. The structures were designed to be produced by the additive manufacturing technology as SLM with a titanium alloy material Ti6AL4V considering the minimum structure thickness of that technology. In the finite element simulation was considered only a size of 5x5mm of implant with 1mm of layer to the bioinspired structure. The boundary conditions applied was only shear load of 5N considering a full bone integration. Was assumed the trabecular bone properties as a linear and elastic behaviour as the titanium structures. The influence of the interface bio design is observed in the models. The shear and equivalent Von Mises stress are influenced by the geometry of the interface. The results of shear stress in the interface are influenced by the design, the Gecko bio-interface presented the highest value of 4MPa and the spore bio-inspired structure presented the lowest value with a maximum of 2.9MPa a reduction around 27%. A similar behaviour was observed in the Maximum von Mises stress, the bamboo structure presented the lowest value with 2.04MPa and the Gecko biostructure the highest value of 3,84MPa.The results of the study as a comparison study and presented the advantages of a bioinspired interface. Within the limitations of the simulations performed, it was possible to observe the behaviour of the outside layer of implant. In the future step, the model will be implemented considering different active layers for a gradual load transfer.

Abstract ID 86

DEVELOPMENT OF CUSTOMIZED COMPOSITE MOUTHGUARDS TO IMPROVE ATHLETES SAFETY AND COMPLIANCE

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Keywords: Mouthguards design, Contact sports, Jaw impact, Injury risk, Athletes comfort, Explicit FEA

Summary: Athletes of competitive sports are at risk of contact induced injuries such as dental and cranial tissues damages. From a biomechanical perspective, a shock to the jaw can directly introduce destructive stress on the tooth-bone complex and indirectly cause traumatic cerebral tissue deformation due to the consequent head kinematical response. Mouthguards (MGs) can be beneficial in reducing the injury risk by changing the dynamics of an impact to the jaw as well as enhancing head stability. Despite availability of three types of MGs (e.g., off-the-shelf, mouth-formed and custom-made), literature findings suggest that only well-designed customized MGs can provide trauma-protective effect and athletes comfort simultaneously. Indeed, not only mechanical properties of materials could have an impact on MG performance, but also the geometrical/structural attributes are contributing factor in the MG design. To study the effect of MG thickness, materials and structural design, an anatomical human head finite element model was developed including skull, teeth, and periodontal ligament. We then evaluated the role of different design variables in the performance of customized MGs by simulation of a Hockey puck impact (using LS-DYNA explicit solver) and analysis of protected teeth response with different MG configurations. We consistently observed that the larger MG thickness is more efficient in reducing the risk of injury in all examined configurations. However, athletes are reluctant to use bulky MGs due to the perceived discomfort, despite being aware of their protective advantage. Additionally, we found that space inclusion is only effective when a hard insert is employed in the composite MG arrangement to distribute the load. Moreover, combination of hard and soft layers could not significantly change the protective performance of MG compared to conventional design when the teeth are in full contact with the MG. The best configuration was obtained when we employed a stiff thermoplastic layer in conjunction with hard and soft rubbery layers in a composite MG with space inclusion in front of incisors. Specifically, it was found that the thickness reduction of a composite and spaced MG from 4 mm to 3 mm is not significantly altering its protective capability. However, it was not possible to find a compromise between protective performance and athletes comfort when the MG thickness was further decreased to 2.5 mm. It was also shown that by controlling the thermoplastic layer's geometry and degrees of hardness, the protective performance of the composite and spaced MG could be tuned.

Collectively, the high cost, long lead time and rare availability of expert orthodontists for fabrication of spaced and composite MG designs with specific structural and material properties could restrict their usage among athletes. However, the operational difficulties in the traditional fabrication process (thermoforming technique) could be by-passed by emerging digital based additive manufacturing technologies. In particular, multi-material 3d printing could present important potential to enhance the design details and the final product's geometrical accuracy. We therefore envision the future with printable composite custom-mouthguard with distinct attributes that are adaptable by the user based on the level/type of competition and associated harshness of the impact incidences.

Abstract ID 87

TRACHEOBRONCHIAL STENTS PERFORMANCE ANALYSIS

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Keywords: Stent, Tracheal, Tissue Engineering, Homogenization

Summary: Tracheomalacia is a disease characterized by flaccidity of the supporting tracheal cartilage, and consequentially by a stenosis, or a tracheal collapse when respiratory volume increases, for instance with cough. With a large stenosis, patient could have breath and eating problems. Tracheal cancer and traumatic lesions, could also lead to stenosis. Tracheobronchial stents are a common procedure in patients with tracheomalacia. However, silicone stents have some performance limitations related with implant migration, development of granulation tissue and accumulation of secretions. On the other hand, implant performance is strongly related with stent geometry and its accommodation with the patient. Additionally, this accommodation is also related with studs geometry, position and number. In fact, different studs are used by manufacturers, but stent performance limitations still persist. In order to study stents performance, a comparative finite element analysis was performed. Granulation tissue formation is related with contact stresses between stent and tissue, migration is related with interface movements. So, swallowing simulations is performed, since this complex movement in the digestive system also creates a complex adaptation on tracheal tree. This analysis is computational complex, due to significant displacements and due to tracheal properties. In fact, airway cartilage rings, annular ligaments and muscle membranes should be considered, however, the analysis complexity increases. To reduce computational time and complexity, equivalent material properties were obtained with homogenization method. Consequently, two sections were considered, a proximal part with more cartilage and less ligaments and the rest with annular ligaments and cartilage rings. Results showed that granulation tissue formation and stent migration depend on studs' geometry and number. So, the optimum performance is difficult to achieve, but a multi-criteria optimization procedure could be a good approach in order to develop new stud designs.

Abstract ID 89

EFFECT OF TOTAL HIP ARTHROPLASTY ON HIP RANGE OF MOTION AND ASSOCIATED MUSCLE FORCES

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Keywords: Hip Osteoarthritis, Total Hip Arthroplasty, pre and post surgery gait

Summary: Hip Osteoarthritis (HOA) is a common chronic joint condition responsible for significant pain and disability. Clinicians recommend total hip arthroplasty (THA) to relieve pain in patients with severe HOA. Walking generally improves after surgery, however, limited restoration of physical function may result after THA and the functional gains do not necessarily reach magnitudes equivalent to those in healthy control populations or correlate well with patient-reported measures of functional recovery post-surgery. Moreover, large deficit in gait speed, stride length, sagittal hip range of motion (ROM), coronal plane hip abduction, and negligible changes in transverse plane hip ROM, deficiency in single limb support time, are reported in patients post THA as compared to healthy controls. Additionally, when patient operated legs are compared to those of healthy subjects at 4 to 5 years post-surgery, reduced hip strength and ROM in flexion, extension, and abduction on operated leg were reported. HOA patients have also demonstrated significantly lower gluteus maximus muscle volume. Additionally, study by Grimaldi et al 2009 has reported variation in gluteus muscle cross-section due to HOA. Significantly lower muscle strength and muscle size in affected leg for HOA patients has been condensed by Loureiro et al. review 2013.The gluteus Medius and gluteus Maximus muscles assist in hip abduction/adduction, flexion/extension, and lateral rotation. Muscle activation and muscle physiological cross-section area both contribute to muscle force generation. The increase in muscle activation reported by Dwyer et al 2014, and the significantly lower muscle size in affected leg for hip OA patients as compared to controls, highlight the need to assess the muscle forces generated at pre- and post-surgery stage of THA. This study calculated hip joint angles in sagittal, coronal, and transverse planes, and predicted forces in the gluteus Medius and gluteus Maximus muscles using a full body musculoskeletal model available in AnyBody software repository (v 7.3.1, AMMR 2.3.1). Gait kinematic data for healthy, 17 right HOA and 13 left HOA subjects at pre- and 6 months post-surgery stage was adopted from the dataset published by Laroche et al. (year?). The model was scaled to patient weight and height and the kinematic motion data provided as an input. An inverse kinematics analysis predicted hip joint angles in 3 planes, and an inverse dynamic analysis combined with muscle recruitment algorithm computed muscle forces. As part of the preliminary investigation, patients with right HOA at pre-surgery stage have reported gluteus Medius muscle forces lower than controls on the affected side and higher on the contralateral side and vice versa for gluteus maximus muscle forces. Whereas left HOA patients have higher gluteus Medius and maximus muscle forces irrespective of the side. A significant variation was reported only in flexion-extension range of motion on the affected side when Wilcoxon signed-rank test was used and no significant variation was reported in the maximum muscle forces at gluteus Medius and Maximus muscles.

Abstract ID 94

UNSUPERVISED HIERARCHICAL AND NON-HIERARCHICAL CLUSTERING TECHNIQUES ON BIOMECHANICAL VARIABLES FOR LONG AND SHORT COUNTERMOVEMENT COMPARISON WITH NO COUNTERMOVEMENT

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Keywords: Unsupervised learning, clustering, countermovement

Summary: Muscle stretch shortening cycle (SSC) is a natural human action with preceding eccentric stretch for efficient submaximal and powerful maximal concentric contraction. At lower limb muscle SSC can be observed on gait, running, and jumping, with higher expression and accessibility of in-vivo SSC at standard maximum vertical jump (MVJ) the most adequate for comparison of long SSC on countermovement jump (CMJ) and short SSC on drop jump (DJ) to squat jump (SJ) without SSC. Despite each form of standard MVJ presents typical movement characteristics and biomechanical parameters with subjects instructed to perform specific MVJ type, DJ and SJ jumping style can resemble CMJ trial, with the need to detect cluster structures based on kinematic and dynamical variables, explaining MVJ trial grouping on elite (E) and non-elite (NE) subjects. For this purpose, clustering analysis was performed on detailed data communities of (i) time-force-impulse, (ii) force-velocity-power and (iii) force-displacement-work in a total of forty-six variables. Whole body center of gravity data was considered from best MVJ repetition of each SJ, CMJ and DJ trials on non-elite group of nNE=6 male sports students without specific train or sport modality (S1-S5) and elite group of nE=16 athletes of the Portuguese national volleyball male team (S1-S16). Hierarchical method with Ward average linkage was applied to each variable community on E and NE groups, separately and jointly considered, to determine the number of clusters and its centroids applying non-hierarchical k-means algorithm to obtain optimal clusters. Agglomeration schedule was used to describe combined cluster on each stage with linkage between groups and squared Euclidean distance computed after Z-scores standardization, along with dendrogram to represent aggregation process and rescaled distance of cluster combine. Time-force-impulse variable community presented on E and NE groups jointly considered as well as E group clear clustering on SJ, CMJ and DJ than NE with S5-CMJ preferable cluster to SJ. Force-velocity-power variable community presented at NE group mixed clustering of SJ and CMJ trials, whereas E group and joint E and NE group presented clear clustering of SJ, CMJ and DJ. NE group presented on force-displacement-work initial clustering on SJ, as well as on CMJ with subsequent SJ and CMJ cluster combined with DJ. As regards to E group and jointly E and NE groups the force-displacement-work variable community presented clear clustering on SJ and CMJ, with exception of NE-S5 SJ and CMJ early cluster,

and final SJ-CMJ agglomeration with DJ. Global set of time-force-impulse-velocity-power-displacement-work variables presented on E and NE, individual and joint groups, three cluster agglomeration corresponding to SJ, CMJ and DJ without case exception. Optimal clusters from non-hierarchical k-means algorithm conduced to distinct cluster centroids on each E and NE group and data community. Presented method conduced to detection of different clusters associated to each MVJ type and data community, pointing clustering as an adequate method explaining SJ, CMJ and DJ trial grouping on E and NE based on kinematic and dynamical variables. Hierarchical and non-hierarchical clustering proved as an adequate unsupervised learning tool capturing MVJ biomechanical group differences and similarities.

Abstract ID 96

IMPLEMENTATION OF A 2D MUSCULOSKELETAL MODEL FOR THE ANALYSIS OF HUMAN MOVEMENT USING FULLY CARTESIAN COORDINATES

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Keywords: Fully Cartesian Coordinates, Musculoskeletal Modeling, Multibody System Dynamics, Hill-type muscle model, Planar muscle models

Summary: Fully Cartesian Coordinates (FCC) formulation is a novel approach to analyze multibody systems [1] that joins the advantages of the Natural coordinates formulation, which defines all the segments of the model solely with the Cartesian coordinates of points and unit vectors [2], and the Cartesian coordinates formulation, which defines each rigid body independently of the remaining bodies of the system [3]. Hence, FCC formulation presents several computational advantages when applied in the analysis and simulation of complex systems, since the constraint equations are, at the most, quadratic, meaning that their contributions to the Jacobian matrix and right-hand side vectors of velocities and acceleration are either linear or even constant in certain circumstances. Moreover, FCC allows for an easier systematization of the modelling process [1], making this analysis approach particularly suitable for the study of biomechanical models. Nevertheless, the FCC formulation has not yet been applied to the kinematic and dynamic analysis of complex musculoskeletal models. This work addresses the computational and modelling aspects of the application of the FCC formulation to the inverse dynamic analysis of planar musculoskeletal biomechanical models where the calculation of the redundant muscle forces is required. A planar lower body musculoskeletal model composed of 6 segments was implemented using the FCC formulation. Each of the 14 lower leg musculotendon units was modeled as a Hill-type muscle model, with a rigid tendon, and integrated in the equations of motion of the system as a generalized external force. The computational muscle model parameters were linearly scaled from the anthropometric dimensions of the subject under analysis, and muscles' paths were defined using muscles' origin, insertion and via points. Muscle activations during the inverse dynamic analysis of five gait cycles, from one healthy subject were estimated by means of a static optimization in which the two cost functions presented respectively by Crowninshield & Brand [4] and by Rasmussen et al. [5], were used. An experimental protocol composed of 38 retroreflective markers [6], an infrared marker-based motion capture system and three force plates were used to acquire the kinematic and kinetic data. No problems were found regarding the modelling procedure and the convergence of the formulation for both the kinematic and dynamic analysis of movement with the inclusion of the redundant musculotendon units. The kinematic and dynamic results were similar to the ones reported in literature. Fully Cartesian Coordinates was successfully applied to analyze planar musculoskeletal biomechanical systems where the calculation of the redundant muscle forces is required. Since FCC combines the major advantages of the Natural and of the Cartesian coordinates formulations, it simplifies the description of the system topology, which increases the systematization of the modelling procedure and avoids coupled matrices. External forces and moments can also be easily applied to the system's elements. Hence, musculotendon

units can be efficiently included in the equations of motion of the biomechanical system as external forces, in which the Hill-type muscle model is embedded. The value of these forces can be successfully calculated by means of static optimization procedures and physiological cost functions.

Abstract ID 98

NETWORK MODELLING FOR NUCLEUS PULPOSUS CELL ACTIVITY IN EARLY INTERVERTEBRAL DISC DEGENERATION

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Keywords: intervertebral disc degeneration, nucleus pulposus cells, chondrocyte, inflammation, network modelling

Summary: Low back pain (LBP) is a major cause of disability worldwide. It is often related to intervertebral disc (IVD) degeneration (IDD), characterized by loss of water, proteoglycans, and type-II collagen, in the nucleus pulposus (NP) of the IVD. Extracellular matrix (ECM) degradation results from complex biochemical processes, with redundant and feedback-looped processes that further interact with physical factors. Accordingly, IDD has a strong inertia and might only be tackled if apprehended sufficiently early. While its pathogenesis remains poorly understood, several numerical and experimental models explore underlying biomechanical and biochemical processes. Yet, the integration of knowledge about IVD cell regulation in health and disease still needs to be improved. Accordingly, a new NP cell (NPC) regulatory network model (RNM) is presented, incorporating critical biochemical interactions in IVD regulation. First, a unique corpus of 120 articles was built about the biochemical stimuli in the NP and their activation and/or inhibition effect on the regulation of soluble cytokines, proteases, and ECM proteins by NPC. Due to the limited knowledge about IDD and the lack of experiments with healthy human IVD material, the corpus was enriched through the STRING database, including general protein-protein interactions in Homo Sapiens. In particular, relevant interactions in chondrocyte regulation were retained. To build the RNM, proteins were represented as nodes that interacted among each other through a directed network of inhibition and activation edges. Nodal activations were calculated through a system of ordinary differential equations that semi-quantitatively interpolates Boolean rules and provide the stable steady states (SSS) of the RNM. Finally, two experimental studies, using healthy human and bovine IVD NPC, were simulated to evaluate the model. Simulations revealed an anabolic basal SSS of the RNM . According to the experimental measurements related to the simulated NPC perturbation, initial activation of IL-17A enhanced slightly COL1A and MMP13, while inactivating almost completely the anabolic ECM components, indicating its negative role in the IVD regulation. In contrast, initial activation of GDF5 up-regulated not only the expression of ACAN and COL2A, but also important growth factors and anti-inflammatory cytokines that play an important anabolic role in the IVD. Interestingly though, the increase of MMP-13 activation with IL-17A was very low, which seems to be supported by some evidence that this protease might not play a clear role in IDD, in contrast to osteoarthritis. Further experiments with anti-inflammatory IL-4 and TGF-B showed a significant increase of the anabolic factors and a decrease but not depletion of the catabolic ones, emphasizing the complexity of the IVD regeneration. IL-1B initial activation increased the activation levels of ADAMTs, the primary enzymes that cleave proteoglycans in IDD progression, whereas the activation of MMP3, believed to

increase in advanced stages of IDD, remained low. Despite, the relatively limited amount of knowledge about IDD, compared to other diseases, e.g., such as osteoarthritis, an enriched RNM was built and successfully assessed against independent experiments. This directed RNM in IDD stands for a unique basis to further integrate both mechano-regulation and biochemical knowledge and enrich existing dose-dependent NPC activity model.

Abstract ID 99

TOWARDS A REPOSITORY OF PATIENT-SPECIFIC INTERVERTEBRAL DISCS FINITE ELEMENT MODELS

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Keywords: intervertebral disc, patient specific, non-rigid registration, finite element analysis, biomechanics

Summary: Numerical analysis methods, such as Finite Element Analysis (FEA), have been widely used to study the biomechanics of human tissues and organs. However, patient-specific (PS) model creation usually requires complex procedures that are difficult to automatize in some instances. For example, in spine computational studies, intervertebral disc (IVD) modeling requires structural meshing, as the synchronized mechanical behavior of specific tissue domains needs to be explored under large deformations. Multiple studies related to IVD degeneration (DD) have been carried out using FEA, but a repository of IVD PS models has not yet been created to explore in-depth PS particularities. A significant challenge is the ability to map different tissue regions, such as the Cartilage Endplate (CEP), Annulus Fibrosus (AF), Nucleus Pulposus (NP), and the Transition Zone (TZ) in PS IVD shapes. Such mapping can provide further information about the influence of the CEP on DD combined with the effects of different sets of diffusion distances from the peripheral vasculature to the NP. This work aims to generate a repository of PS finite element meshes of IVD models with the same mesh connectivity and different geometries of the external surface and its internal components for systematic mass FEA. Using T2-weighted magnetic resonance images, 176 PS IVD models were obtained through 3D segmentation, acquired during the European project My Spine (FP7-269909). Segmentations included the AF and NP. The Bayesian coherent point drift (BCPD) algorithm was used to non-rigidly align the meshes. This code fits a point cloud of a source mesh (template) to a target mesh (segmentations). In this way, a pre-existing structural mesh of an IVD was adapted to the PS models. The external surfaces of the AF and NP were represented by point clouds, which were used as targets. The morphing process of the template was carried out in three stages. First, the AF and the NP surfaces were adapted. Then, the results were merged into a single point cloud, used as a target, for the final fitting of the complete volumetric mesh of the template. The CEPs, not visible in the images, were automatically recreated, with a thickness between 0.7 and 1 mm. The development of the second stage preserved the surface area initially covered in the IVD. Mesh quality of the morphed models and Euclidean distance between the morphed and the target were checked to ensure good quality elements. A repository of finite element meshes with the same connectivity was created following the abovementioned method. Regarding mesh quality, the average criteria limits of all morphed IVDs were: Min and Max angle on Quad Faces (<10 and >160) were less than 0.2 and 0.8 % of the total elements, respectively. The Hex elements that exceeded the Aspect Ratio criteria limit (>10) were less than 6%.This repository is a unique

set of model collections to explore the effect of multiple geometrical variations on the IVD multiphysics and mechanobiology, including the likely substantial impact of the CEP. The algorithm can generate PS FE models from any segmented surfaces third parties provide.

Abstract ID 100

PREDICTION OF GROUND REACTION FORCES DURING RUNNING

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Keywords: Running, Inverse Dynamics, Biomechanical model, Ground Reaction Forces

Summary: Although research on running biomechanics has been increasing in popularity, some restrictions, especially regarding data acquisition, limit the development and application of computational models. While some alternatives exist to the use of stereography for collecting the human body kinematics, such as marker-less approaches, the same cannot be said of the methodologies used to measure ground reaction forces (GRF). Well established gold standard techniques in this field are force platforms, and both instrumented walkways and treadmills. However, these approaches are restricted to the laboratory setting, when available as they are expensive, and are not portable. Pressure insoles can overcome some of these methodologies' shortcomings, but there have been studies that describe clear differences in the shape and magnitude of the force curves when compared to force platforms. Moreover, frequent need of calibration and the lower sensitivity make the pressure insoles an unreliable alternative to measure GRF during running. Previous computational studies were able to estimate GRF using kinematic data and a biomechanical model of the human body, but the foot was modelled as a single rigid body. To the authors' best knowledge, the effect of the addition of degrees of freedom (dof) on the foot regarding the GRF estimation remains unknown. This work proposes an upgrade to the existing computational procedure used to estimate GRF quantification, while considering a complex foot structure. To this end, a full-body musculoskeletal model composed of 18 rigid bodies was created. The arms, forearms, head and trunk, pelvis, femora, patellae, tibiae, tali, calcanea and toes were constrained by spherical and revolute joints, totaling 25 dof. The movement of the patella was simplified, and it was considered rigid in relation to the femur. The muscle system included 80 muscle-tendon units with their contraction dynamics represented by a Hill-type muscle model. The GRFs are estimated by solving the Newton-Euler equations of motion, along with the indeterminate problem of muscular redundancy using Inverse Dynamics, an optimization routine, and a dynamic contact model. This dynamic contact model includes several contact elements on each foot of the musculoskeletal model and a strength profile attributed to each one. Kinematic data, required for the application of the developed methodology, were acquired at the Laboratory of Biomechanics of Lisbon. Subjects, with no story of musculoskeletal disorders, walked and ran at a self-selected speed over floor mounted force platforms for verification of the methodology. The markers were placed according to the ISB recommendations and were used to drive the musculoskeletal model. This method was applied to all subjects and compared to measured force plate data. Preliminary results showed that the proposed methodology was able to estimate GRFs that were consistent with the data from the force plates. The joint reaction forces, joint torques, and muscular activations estimated through inverse dynamics were also consistent with

the literature. The proposed method is expected to be a valid alternative to the use of force plates in laboratorial settings, allowing for a higher flexibility of GRFs acquisition while still maintaining high accuracy.

Abstract ID 101

GRAFT POSITIONING IN SUPERIOR CAPSULAR RECONSTRUCTION: COMPUTATIONAL ANALYSIS OF GRAFT INTEGRITY AND SHOULDER STABILITY

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Keywords: Rotator cuff tear, Arthroscopic superior capsular reconstruction, Fascia lata graft, Shoulder stability, Musculoskeletal model

Summary: Arthroscopic superior capsular reconstruction (ASCR), for the treatment of irreparable rotator cuff tears (IRCTs), has been shown to produce excellent clinical outcomes. However, graft tear rates can range from 4.2% up to 75%. The position of the shoulder during graft fixation may affect the outcome of the procedure, possibly in different forms depending on the type of IRCT. But this topic lacks biomechanical evidence. The aim of this study was to evaluate the influence of the positioning of the graft in ASCR on shoulder stability and graft tear risk. A 3-D musculoskeletal model of the upper limb was modified to account for the fixation of the graft in ASCR. A total of 126 shoulder positions for graft fixation were evaluated. The material properties of the graft were defined based on previous experimental data of fascia lata graft constructs. The effect of the long head of the biceps tenotomy was also studied. Two biomechanical parameters were used to evaluate the integrity of the graft and shoulder stability: the graft strain and the glenohumeral joint reaction force (GH JRF), respectively. The statistical analysis was based on analysis of variance (ANOVA) and multiple comparison. The level of significance was set to $p < 0.05$. For abduction angles above 15° during fixation, the graft had a high risk of tearing when the arm returned to the side of the trunk, considered as the resting position. For abduction angles below 15°, the mean shoulder stability after graft fixation improved significantly, ranging between 6% and 20% ($p < 0.001$), for a IRCT affecting the supraspinatus tendon. Also, for this RCT tenotomy significantly decreased shoulder stability after ASCR ($p < 0.007$).This study showed that the position of the shoulder, during graft fixation, affected both graft tear risk and shoulder stability, after ASCR for the treatment of RCTs. ASCR also improved shoulder stability, compared to the preoperative condition, regardless of the shoulder position. This study provides important insight regarding the role of position of the shoulder during graft fixation.

Abstract ID 105

THE INFLUENCE OF HYPER-ELASTIC MATERIAL PROPERTIES ON MECHANICAL STRESS IN CAROTID ARTERY PLAQUES: A 3D STRUCTURAL SIMULATION ROBUSTNESS STUDY

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Keywords: Carotid; Structural Stress; Stress; VSS; Hyperelasticity; Robustness; Mooney-Rivlin; Biomechanics; MR

Summary: Mechanical stress within carotid atherosclerotic plaques have been shown to complement traditional methods such as luminal stenosis in assessing plaque vulnerability and predicting clinical presentation. However, the sensitivity of stress predictions to the modelling strategy has not been widely assessed. The vessel structural stress (VSS) calculation may be impacted by uncertainties from a number of sources, namely: i. Image acquisition quality and parameters, ii. Image segmentation accuracy, iii. Model boundary and loading conditions, and iv. Material properties. The choice of material properties for the arterial wall and plaque components is a major uncertainty, and these cannot be directly determined using *in-vivo* methods. The aim of this study is therefore to relate the impact of the uncertainty associated with the material properties to what extent the structural stress may be considered a useful clinical biomarker based. Model reconstruction has been carried out from multi-slice, high resolution magnetic resonance *in-vivo* carotid artery images, and 1-way-FSI simulation has been performed, culminating in a solid-only simulation with pressure loading from the CFD simulation applied to the lumen wall of the solid model which includes the vessel wall and plaque components. This process was repeated using an inverse pressurisation algorithm to obtain a more accurate estimation of the 3D *in-vivo* pressurised state (see attachment). The usefulness of the stress environment to characterise plaque is assessed by computing components of the VSS at locations of interest, such as within diseased regions susceptible to rupture. The models and plaque were modelled by a modified Mooney-Rivlin Strain Energy Density Function (SEDF), with three unknown variables (see attachment).The likelihood of critically high stress within a baseline model is assessed by measuring VSS at different locations on plaque and computing the result of running a number of simulations using randomised sampling of the SEDF coefficients. In the 3D simulations, it has been shown that stress can be an important determining factor of symptomatic plaque when comparing patients with both single-sided as well as bilateral stenosis. Additionally, the uncertainty associated with material properties used to model the vessel wall can have a significant impact on the derived stress environment.

Abstract ID 106

TISSUE THERMAL DAMAGE IS REDUCED WHEN USING INSULATED ELECTRODES IN COMPARISION TO STANDARD ELECTRODES DURING ELECTROSURGERY: A COMPUTATIONAL INVESTIGATION

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Keywords: Electrosurgery, Joule Heating, Soft Tissue, Medical Device

Summary: Electrosurgery is characterised by the passage of radiofrequency electrical current through the patient's tissue, causing resistive heating also known as Joule heating. This results in the elevation of temperatures, thermal damage, and can impair tissue healing. Temperatures can exceed 200°C and depends on electrode design, operating conditions (current density, waveform, and usage time), and tissue electrical and thermal conductivity properties [1, 2]. Electrodes with a side-layer of insulating material may reduce thermal spread in comparison with an uncoated electrode [3]. This reduced thermal spread occurs principally because of current density focusing in the intended direction during application. Empirically quantifying tissue temperature, and damage during electrosurgery has its difficulties: thermographic imaging only captures surface temperatures, thermocouples are inaccurate in RF environments (optical probes are an alternative), and tissue damage assessment requires histological expertise and ex-vivo models will never recapitulate the in-vivo environment. Therefore, in this study, finite element analysis (FEA) is employed to interrogate how the electrode, operating conditions, and tissue properties influence thermal damage in the surrounding tissue, which to date is not yet fully understood. The objective of this study is to develop a computational model which represents electrosurgical cutting with insulated and uncoated electrodes to enhance our understanding of how these primarily geometrical parameters influence electrosurgery. Geometries of an uncoated and insulated electrode were imported into Comsol Multiphysics and 3D models were generated of the electrodes inserted into tissue, reflecting experimental work being carried out in tandem with this work. The electrical potential distribution is described by the quasistatic approximation of the Maxwell equations, $\nabla\bullet(\sigma\bullet\nabla\varphi))=0$, where σ is electrical conductivity, and φ is electrical potential. The time-dependent temperature within the tissue is described using the Pennes bioheat transfer equation without accounting blood perfusion effects (ex-vivo conditions), $\rho c(dT/dt)=\nabla\bullet(k\bullet\nabla T)+q_{em}$, where ρ, c, k, T, and q_{em} are the density, specific heat, thermal conductivity of tissue, temperature and joule heating source term ($q_{em}=\sigma|\nabla\varphi|^2$), respectively. The parameters σ and k are implemented as temperature dependent properties. Electrosurgery in 'cut mode' applies current to tissue at a frequency of 391 kHz and appropriate tissue properties are obtained from the IT'IS database to reflect this [4]. Electrical potential is applied to electrode at physiologically relevant magnitudes obtained

experimentally by differential probing at different electrosurgical generator power settings. A zero electrical potential (φ=0 V) is applied where the grounded pad is located. This study provides unique information regarding the thermal spread surrounding electrosurgical electrodes, which is otherwise difficult to obtain directly through experiments. The results demonstrate the effectiveness of insulated electrode designs for thermal damage reduction. This is comparable to experimental work comparing insulated and uncoated electrodes subjected to robotically controlled electrosurgery [3]. The model developed in this work can inform device design in a time-efficient and cost-effective manner, and help design electrodes for areas of the human body where the reduction of thermal damage is of utmost importance.

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Abstract ID 107

NUMERICAL ANALYSIS OF SINGLE AND MULTI-FREQUENCY CURRENT WAVEFORMS AND THE EFFECT OF OPEN-IRRIGATION COOLING DURING BIPOLAR ELECTROSURGERY

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Keywords: bipolar coagulation, electrosurgery, computer modeling, thermal damage

Summary: Bipolar coagulation is widely used in minimally invasive electrosurgery for neurosurgical hemostasis or tissue removal. The technique makes use of radiofrequency energy delivered in a form of a modulated intermittent current waveform to biological tissue interposed between two closely spaced bipolar forceps. The system offers advantages over monopolar electrosurgery in providing a more localized and precise tissue coagulation and a lower risk of thermal damage into the neighbouring organs. However, tissue adhesion and char formation are the main drawbacks during the procedure, which lead to tissue shearing during electrode removal and delayed tissue healing in regions where excessive carbonization arises. Current waveform and power mode are the main parameters by which heat rate can be controlled during electrosurgical coagulation. Moreover, irrigation-coupled systems have been designed to reduce the temperature response by infusing a low flow cooling fluid to the target tissue [1]. Yet, the coolant can absorb the heat and disperse uncontrollably in tissue, and the appearance of abrupt steam bursts produced in the form of audible pops may additionally displace hot fluid away from the treatment site. Previous studies have developed computer models to investigate the processes involved in heat dissipation in tissue [2][3]. However, little research has been done on tissue thermal response electrosurgery associated with multifrequency waveforms. To the best of our knowledge no computer model has considered an open irrigated cooling system for bipolar coagulation. In this study, 3D FEM models have been built to investigate and better comprehend tissue thermal and electrical response for current waveform modulation, power setting and cooling system involved in bipolar electrosurgical coagulation. Three-dimensional finite element models were developed in COMSOL Multiphysics Software. The problem was formulated as a coupled electrical-thermal analysis accounting for Joule resistive heating and heat convection. The electric and temperature fields were governed by the Laplace equation and the modified bioheat equation, respectively, and temperature dependent tissue properties were considered. The model was informed by the electrical data acquired from an experimental study that was conducted using ideal load (25-1000 Ω) and ex vivo soft tissue samples to characterize current waveforms and frequency spectra (300 kHz - 8 MHz). Bipolar coagulation on soft tissue was carried out at two clinically relevant power settings (7 W and 35 W). Surface temperatures were analysed using real-time infrared thermography and used to validate the computational models. The validated models were applied to investigate modulated

input current for a varying number of frequency components and the thermal effect of open irrigation cooling system. This study demonstrated a computational approach to predict thermal damage evolution in tissue under bipolar coagulation with single and multi-frequency waveforms. The results were supported with the experimental data for characterization of the input bipolar 'coag' signal and surface spatial and temporal distributions of temperature. These results revealed how cooling reduced tissue temperatures during bipolar electrosurgery and offer a useful way for the prediction and optimization of bipolar treatments of soft tissue.

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Abstract ID 108

AN HPC APPLICATION OF PORO-ANISO-HYPERELASTIC MODEL FOR THE IN SILICO STUDY OF THE INTERVERTEBRAL DISC DEGENERATION

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Keywords: IVD degeneration, Biphasic modeling, HPC

Summary: Intervertebral Disc (IVD) degeneration is the leading cause of Lower Back Pain, affecting more than 10% of the global population. In silico modeling could contribute to the understanding of the dynamics of IVD degeneration. Patient specific medical solutions can be explored by exploiting the high scalability of supercomputers, regarding both the number of cases simulated and the refinement level of the finite element mesh. For that reason, finite element simulations are performed in Alya, the highly parallelizable finite element (FE) solver developed by Barcelona Supercomputing Center. IVDs are known to exhibit poro-aniso-hyper-elastic behavior. The mechanical hyperelastic model accounts for the compressibility of the total IVD matrix, while respecting the incompressibility of both the dry matrix and the surrounding solute. The presence of collagen (COL-I, COL-II) is related to the model's anisotropy, for which a modified Holzapfel-Gasser-Ogden model is used. Finally, the pressurization of the disc derives from both the mesh's deformation and the Donnan osmotic pressure. While Alya treats solid models considering a Total Lagrangian formulation, the simulation of both the porous medium and the solute transport are traditionally solved following an Eulerian formulation. To overcome this inconsistency and to account for the deformability of the mesh, a proper set of Piola-Kirchoff transformations regarding the porous model's permeability and the solute model's diffusivity, are employed. This setup allows for high scalability as well as the plug-in of Agent Based models designed for HPC.

Abstract ID 110

INVERSE DYNAMICS APPROACH TO THE BIOMECHANICS OF SWIMMERS USING MULTIBODY DYNAMICS METHODOLOGIES

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Keywords: Movement Biomechanics; Hydrodynamic Forces; Swimming Style; Motion Reconstruction

Summary: Human motion is one of the objects of study in biomechanics, which involves complex interactions between the neuromuscular and skeletal systems. Understanding these interactions is necessary not only for medical applications but also for sports sciences or for planning physical conditioning activities. Fundamental quantities of interest in human motion research are the intersegmental forces and moments acting at the joints, which represent the net loads that act at each biomechanical joint, and muscle forces. Computational biomechanical models based on multibody dynamics are powerful tools that enable the evaluation of these quantities in the human body, whose in vivo or in vitro measurement is, when possible, extremely difficult. In the context of human swimming, current biomechanical models are mostly based on simplified models of specific parts of the human body. Due to limitations on motion acquisition, especially in the air-water interface, they are kept simple and are hardly able to simulate the broad range of motion of many of the anatomical segments relevant to swimming. Another fundamental data for the evaluation of internal forces are the external forces acting on the human body during swimming, herein referred to as hydrodynamic forces. Unlike terrestrial motion where these external forces are easily measured using force platforms, the determination of the external forces in water is very difficult. This work provides a methodology that allows overcoming the difficulty in obtaining the external forces acting on the swimmer, by estimating them using the Swimming Human Model computational tool, SWUM. These forces distributed on the swimmer biomechanical model anatomical segments are used, together with the model kinematics whose movement is acquired experimentally in the swimming pool, to obtain the internal forces in the model. The methodology presented and discussed in this work is applied to a swimmer using a freestyle technique, crawl. The results obtained allow for the evaluation of the internal forces in the human body biomechanical model which are of particular interest to understand what is the contribution of each anatomical segment for the thrust of the swimmer and what are the forces required to develop such movement. In the process, the estimation of the 'joint reaction' forces allows to have an estimation of the health risks to develop this swimming technique.

Abstract ID 112

TPMS SCAFFOLDS FOR BONE-CARTILAGE INTERFACE

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Keywords: Tissue Engineering, Osteochondral Interface, TPMS, Pore size, Design optimization

Summary: The purpose of a Tissue Engineering (TE) scaffold is to provide support for cells to adhere, proliferate and differentiate into a specific phenotype. These cellular phenomena are all dependant of the scaffold design and structural properties like geometry, porosity, pore size, pore interconnectivity and surface area. Therefore, the design and production of TE scaffolds with controlled pore size and distribution represents a classic optimization problem. Within this scope, TPMS (Triply Periodical Minimal Surfaces) scaffolds have been widely used for TE applications due to their ability to form fully interconnected porous structures with controlled porosity and great values of specific surface area (SSA). We are currently expanding our scope to the subchondral bone, which is not a homogenous tissue and allows for the connection between articular cartilage (AC) and the trabecular bone layer surrounding bone marrow. It also provides support for load distribution. Under the eventuality of a chondral defect, literature states that it is important to preserve the interactions between subchondral bone and AC. In fact, our research group has been focused on the study of permeability and pore size of TPMS-based 3D printed scaffolds for bone TE. These are important parameters to assess structural properties but also to quantify important cellular phenomenon such as cell seeding and distribution into the scaffold, macromolecules transport, and cell mechano-regulation stimuli like fluid shear-stress and pressure.
Focusing on pore sizes, the scaffolds we previously produced and characterize had pore sizes ranging from [160, 1015] μm. Literature defends that a mean pore size >300 μm allows for direct vascularization and osteogenic cellular differentiation on scaffolds for bone TE. In contrast, pores smaller than 300 μm might induce chondrogenic differentiation and help prevent vascularization, which is crucial given that AC is an avascular tissue. Therefore, in this work we will present how we can tune different types of TPMS in order to achieve the best combination of structural parameters like cell size, cell number, and pore size that promote the desired osteogenic cell differentiation and proliferation, and control vascularization of the tissue while maximizing SSA, permeability and scaffold's mechanical integrity from implant perspective. Porosity and pore size gradients will be explored for osteochondral interface reconstruction as well as the possible anchoring/interaction with hydrogels for viscoelastic chondral phase repair.

Abstract ID 113

PERMEABILITY AND WALL SHEAR STRESS ANALYSIS IN SMOOTHED VS NON-SMOOTHED TPMS SCAFFOLDS

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Keywords: Triply Periodic Minimum Surfaces, Permeability, Wall Shear Stress, Bone Tissue Engineering, Computational Fluid Dynamic

Summary: When designing scaffolds for Bone Tissue Engineering (BTE) two fundamental characteristics to consider are the permeability of the scaffold and the Wall Shear Stress (WSS) that will affect the cells inside the scaffold. This is because different levels of WSS and permeability lead to different mechanical signals for the cells, which will in turn cause differences to the cellular differentiation process. These parameters are affected by various factors, with the major ones being the scaffold porosity, the scaffold geometry, and the topology of the scaffold surfaces. Accordingly, this study is focused on analyzing the differences in permeability and average WSS, in various Triply Periodic Minimum Surfaces (TPMS) scaffolds, with either smoothed or non-smoothed wall surfaces.
For this study two different TPMS structures were used (Schwartz D (SD), Gyroid (SG)), each one with three different levels of porosity (60%, 70% and 80%), resulting in a total of six different scaffold geometries. For each original geometry, a hexahedral mesh of a single cubic unit was created, alongside an empty chamber before and after the scaffold to allow the fluid flow to stabilize. Afterwards, a Laplacian smoothing step was applied to the inner surface of the scaffolds to obtain the smoothed scaffold geometries in an analogous tetrahedral mesh. Both the original and smoothed design were then studied using FLUENT® ANSYS® (Ansys Inc., Canonsburg, Pennsylvania, USA) to perform a Computational Fluid Dynamic (CFD) analysis to determine their average WSS and pressure difference. After obtaining these results, the permeability values of the scaffolds were calculated using Darcy's law. For these CFD analyses, the parameters chosen for the simulation were a fluid density of 1000 kg/m3; dynamic viscosity of 0.001 Pa.s and an inlet velocity of 0.0001 m/s.
Comparing the average WSS of the original scaffold surface with the analogous smoothed surface, the smoothed scaffolds had an average WSS increase of 26%, considering a minimum of 24.7% for the SG60 scaffold and a maximum of 27.2% for SG80. Regarding the permeability, the smoothed scaffolds had an average pressure drop decrease of 4% when compared to the original scaffold geometry, with a minimum of 3.6% for the SG60 scaffold and a maximum of 4.5% for the SD80 scaffold.
The WSS outputs showed a significant difference between the original and the smoothed TPMS scaffolds, with the smoothed surfaces allowing for higher WSS as theoretically expected. This difference highlights how the original jagged surfaces are not the best option to computationally analyze the average WSS of scaffolds, seeing as the increase

in surface area compared to the smooth scaffold results in a much lower WSS. In contrast, the permeability results showed that, even thou the original scaffold design might not be suitable to study WSS, they present an appealing, lower computational cost method of study the pressure drop (and consequently their permeability) of BTE scaffolds.

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