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Abstracts Topic: Conceptual design and simulation of medical device performance

A Prototype for the Acquisition and Analysis of the 3D Mandibular Movement

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PURPOSE: In Dental Medicine is essential to know the mandibular kinematics to simulate the temporomandibular joints, to position teeth molds in articulators, and to reproduce the mandibular movements to insure a satisfactory occlusion.

Currently, both commercial and custom-made devices are considered expensive and difficult to use in common clinical situations. Considering these disadvantages, a new system was developed for the acquisition, visualization and analysis of the 3D mandibular movement that is economical, easy to use and sufficiently precise.[1,2]

METHODS: The development of the prototype system began with the choice of the technology to use in the 3D mandibular movement acquisition, because the device support structure would strongly depend on it. Hence, electromagnetic sensors were used to measure the magnetic field created by a small magnet placed inside the patient's mouth (near to the incise point).[2]

After choosing the technology to use, it was necessary to design the support structure for the acquisition system.[1] Instead of creating a new device structure, a common facial arc used in Dental Medicine was adapted as the main support structure; thus, we chose the *Arcus* facial arc from *Kavo*.

As the selected arc was primary designed to make static measurements, the first step in its adaptation was the redesign of the pieces that could make difficult the dynamic measurements or harm the patient.[1] Thus, the auricular pieces were redesigned.

For the acquisition of the sensor signals was used a data acquisition device (DAQ) with plug-and-play USB connectivity, the NI USB-6008 model from *National Instruments*.[2]

To make easy the acquisition and analysis of the 3D mandibular movement using a personal computer, was build a new computational application with an adequate graphical interface using the developing tool *LabVIEW* from *National Instruments*.[1,2]

To know the 3D trajectory of the magnet was necessary to convert the output voltage of the 3 electromagnetic sensors used in 3D Cartesian coordinates. To solve this problem, a neural networks approach was used.[2]

RESULTS/DISCUSSION: The prototype system developed has adequate precision and can be produced at low price. So we think that it is a good help for medical doctors to detect and define good treatment plans for problems of dental occlusion.

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Abstracts Topic: Conceptual design and simulation of medical device performance

Implant Alignment And Quality Of Life Following Computer-Assisted Total Knee Arthroplasty: A Prospective Comparative Randomized Multicenter Study

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PURPOSE: Computer-assisted navigation systems have been developed to improve limb alignment of the prosthesis. However, the impact on the well-being of patients has never been evaluated in this context. This prospective study compares the alignment accuracy and impact on quality of life between computer assisted surgery and conventional surgical technique.

METHODS: A total of 300 randomization envelopes were sent to 6 European centers in 3 different countries with a randomization of 1 to 1. Radiologic as well as clinical data (SF-36 and KSS scores) where collected preoperatively as well as 6 weeks and 6 months postoperatively. For navigated patients, displayed HKA values were noted at surgery to correlate intraoperative values to postoperative x-rays. Complications were noted during the 6 month follow-up.

RESULTS: A total of 295 patients were included in the study, 148 with computer assistance, 147 with conventional surgery. All patients were followed for 6 months.

The proportion of patients with a mechanical axis with more than 3° of varus/valgus was significantly less in the navigation group at 6 weeks ($P = 0{,}01$) and 6 months ($P = 0{,}04$). Similar results are found for the femoral component at 6 months ($P = 0{,}001$).

At 6 months, the progression in SF-36 scores was significantly better in the computer assisted group, bodily pain ($P = 0{,}03$), physical health dimension ($P = 0{,}01$), mental health dimension ($P = 0{,}005$) and global SF36 score ($P = 0{,}002$). While a difference in operating time was noted ($P < 10^{-5}$), the blood losses where similar for both groups ($P = 0.8$).

CONCLUSIONS: This is the first ever prospective study focusing on patient well-being. Computer assisted surgery improved the accuracy in total knee arthroplasty. Most importantly, at 6 months, patients had less pain and better SF-36 scores in the computer assisted surgery group.

Level Of Evidence

Level I: High-quality randomized controlled trial with statistically significant difference.

Abstracts Topic: Geometric modeling from medical images

A Virtual MRI System

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PURPOSE: MRI is established as an important component of medical diagnostics, but is also developing a role in interventional and intraoperative procedures. There is therefore an increasing need to introduce virtual MRI into the medical simulation ecosystem where it can interact with other virtual entities. For instance, with this approach it becomes possible to obtain virtual MRIs of virtual patients undergoing virtual interventions. Some of the potential applications are: verification of virtual tissue models; surgical training for MR-guided interventional MRI procedures; training of MR operators and users of MR data during interventional and intraoperative procedures; virtual development and evaluation of image-guided procedures.

METHODS: Our approach to virtual MRI is the construction of an integrated device that is both a real MRI and an MRI simulator. The 2 modes complement each other – virtual MRI and real MRI can be evaluated against each other in a range of scenarios. Very precise and verifiable virtual MR images can be produced, due to the full physics simulation employed, including RF and static field maps. Tissue models including MR properties[1] are used as input to the virtual image production process.

The device consists of a magnetic resonance (MR) research console with a full-function hardware-independent pulse programming environment, and a parallel computer cluster running Bloch equation simulations on a 3D digitally-defined spin phantom. The system is designed to allow precise side-by-side comparisons of experiment against theoretical predictions for real-world, complex pulse sequences. The simulator has broad modeling capabilities including: spin relaxation, motion, diffusion, RF and static field inhomogeneities, waveform distortions, instabilities and noise, and functions for arbitrary pulse sequences. The simulator can employ multiple spins per voxel, which allows both the development of stochastic tissue models and the simultaneous simulation of multiple physical phenomena. Simulation speed for the full-physics simulation is accelerated by the use of parallel processing and by use of parallel MR imaging techniques. For applications where speed of simulation is paramount it is possible to omit the full physics simulation, yet retain realistic images, with some limitations.

RESULTS/DISCUSSION: Integration between real and virtual MRI provides a link between the real and virtual worlds. It allows presentation of the virtual medical training world in a format familiar in the real hospital environment. Results will be presented for both high field 9.4 Tesla and low field 0.2 Tesla MRI systems.

The benefits of an integrated general-purpose simulation system are many. They include technique verification, investigation of artifacts and model development. There are very many applications in biomedical MR for this dual approach of generating both real and virtual data, ranging from simple troubleshooting, to verification of quantitative measurements, through to scientific discovery. The use of the system reduces costs by saving time during development, and allowing off-line development and test.

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Abstracts Topic: Geometric modeling from medical images

Creation of Finite-Element Models from 3-D Imaging Data

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PURPOSE: The geometries of 3-dimensional models of anatomic structures can be created de novo or they can be extracted from various types of 3-dimensional imaging data: x-ray computed tomography, magnetic-resonance imaging, histologic sections, ultrasound, etc. In the latter case, the segmentation of structures of interest can be very time-consuming, especially when there are multiple interconnected structures with different properties. If the models are to be used for finite-element simulation, the mechanical connections among different structures must be explicitly and consistently defined and the meshing must be well controlled.

METHODS: Software is presented for creating 3-dimensional finite-element models from various types of imaging data. Image segmentation is done with a combination of manual tracing and interactively guided automatic tracing and smoothing. Connections and shared surfaces are defined explicitly by means of a graphical interface, as are visual properties, physical properties, boundary and load conditions and mesh resolution. Different model subsets can be defined with different properties. Multiple models can then be generated with, for example, different mesh resolutions for finite-element convergence testing.

RESULTS/DISCUSSION: The software has been used to create models for finite-element simulations[1] as well as for visualization and quantification[2] and for teaching.[3] The software is available for different operating systems, and can be downloaded from http://audilab.bmed.mcgill.ca/~funnell/AudiLab/sw/.

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Towards Computational Design of 3D Scaffolds for Cell-Based Gene Therapy

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PURPOSE: Biomaterials capable of efficient gene delivery by embedded cells provide a fundamental tool for treatment of diseases. Maintaining adequate nutrient/oxygen diffusion to cells within the biomaterial is essential for cell survival.[1] Based on these hypotheses, this presentation will focus on development of 3D macro/microporous scaffolds, by combining the 3D-plotting and porogen leaching techniques. The in vitro results for poly-L-Lactide (PLLA) scaffolds seeded with murine bone marrow-derived mesenchymal stromal cells (MSCs), genetically engineered to secrete erythropoietin (Epo) will be presented. This talk will also give an overview on computational design of these constructs targeting optimal scaffold architectures to control in vivo drug delivery.

METHODS: The plotting material was prepared by dissolving PLLA in methyl ethyl ketone, and subsequently mixing with 10 to 50% wt/wt of salt particles (NaCl, 30–75 μm). The plotting material was transferred to a bioplotter from Envisiontec and dispensed layer by layer forming 0°/90° strand layout and controlled pore size of 150 μm. The scaffolds were then washed and vacuum-dried to extract the porogen and remove the solvent. Macroporous scaffolds (no porogen) were used as controls. Unconfined compression tests were conducted on scaffolds in a saline bath to estimate the compressive stiffness. MSCs were isolated from female 15–20g C57Bl/6 mice (Laprairie Co) and then genetically engineered by several rounds of retroviral transduction with filtered retroviral particles from subconfluent GP+E86 cells previously transfected to express the cDNA for murine Epo.[2] The sterilized scaffolds were coated with gelatin (1% in PBS) and seeded at a cell density of 1×10^6/ml. The constructs were then cultured for 2 weeks and removed at specific time points for evaluation of adhesion, proliferation and viability (n=4). The Epo secretion was quantified by an ELISA kit (Roche Diagnostics). The attachment and growth of MSCs were examined by scanning electron microscopy (SEM) and histologic study, and the cell activity by MTT assay.

RESULTS/DISCUSSION: SEM images following 2 weeks of static seeding showed cell attachment onto and between the strands. Hematoxylin-Eosin staining revealed a uniform distribution of cells within the scaffolds at the highest microporosity (50% salt). Cell viability was enhanced with increasing microporosity most likely because of more efficient oxygen/nutrients transport within these constructs. After one week of culture, the genetically engineered MSCs demonstrated a 2 fold increase in Epo release within micro/macroporous scaffolds compared with macroporous constructs ($P < 0.05$). This was attributed to the enhanced cell viability in the presence of micropores.

CONCLUSIONS: This study showed that the macro/microporous constructs can promote cell viability and release of therapeutic proteins, and demonstrated their capacity for a dual role, as scaffolds for tissue regeneration and as delivery systems for soluble gene products.

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A Multi Level Computational Modeling for Quantifying Cell Deformation in Encapsulated Alginate Structures

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PURPOSE: In this study, the stresses and deformations of encapsulated cells under compressive loads are quantified via a multilevel nonlinear finite element approach. The macro-level model is used to mechanically characterize the alginate-cell construct. At the microlevel, the effects of alginate concentration, cell model, and the microlevel geometric heterogeneity on cell deformation are examined. Cells are modeled as single phase inclusions containing only a nucleus phase; then as a 2 phase inclusion comprising of a nucleus phase and cytoplasm phase. This study also analyzes the effects of 2 geometrical parameters namely cell size and cell distribution on the local stress levels of the cell. Subsequent statistical analyses provide insight for the degree of influence from these factors.

METHODS: The analyses were conducted via a multilevel nonlinear finite element method. The macro-level analysis is a nonlinear finite element model that characterizes the macroscopic behavior of alginate discs with encapsulated endothelial cells under load. Upon the results of the macro analysis, a microlevel analysis is conducted to determine local stress/strain fields in a selected region with the encapsulated cells. Numerical results are determined and analyzed to quantify the effects from various sources on the local cell responses.

RESULTS: The study shows that cells embedded in a higher alginate concentration (3%wt/vol) would experience higher stress levels when compared with cells embedded in a lower alginate concentration (1.5%wt/vol). Furthermore, the analysis of the geometric heterogeneity indicates that there is much higher stress concentration in areas where cells are clustered together compared with the areas where cells are relatively isolated.

DISCUSSION/CONCLUSIONS: We first focus on quantifying the effects of micro physical and geometric heterogeneity on the endothelial cells encapsulated in alginate gel under load, via the multilevel finite element approach. The microlevel stresses and deformations that cells are subjected to under macro-level loads are analyzed. Secondly, we examined the modeling of the cell, with and without a distinction between the cytoplasm and nucleus in terms of material properties. From the single phase model, the cell can withstand higher stresses since the nucleus is much stiffer than the cytoplasm. However, to look into cell damage, it becomes imperative to identify the stresses at the cytoplasm which is much less stiffer than the nucleus. Additional information obtained from the detailed model may be linked to membrane damage and cell injury. Finally, this study also analyzed the effects of 2 geometrical parameters namely cell size and cell distribution on the local stress levels of the cell. This further enables us to understand the differences in terms of stresses and deformations at the cellular levels when cells are isolated versus a state when cells form clusters.

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