Study of bone implants based on 3D images

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Abstract

New medical input technologies together with computer graphics modelling and visualization software have opened a new track for biomedical sciences: the so-called in-silice experimentation, in which analysis and measurements are done on computer graphics models constructed on the basis of medical images, complementing the traditional in-vivo and in-vitro experimental methods. In this paper, we describe an in-silice experiment to evaluate bio-implants for bone regeneration: data capture and graphical algorithms. The results show that computer graphics models can give similar measurements than the traditional methods using the same precision with additional advantages such as the capability of choosing the best, or even several, plane orientations to do the study. There are also the intrinsic advantages of animal sacrifices reduction and sample preservation.

1 Introduction

An important research in the biomaterials field is the synthesis of materials capable of simulating the regeneration and repair of biological tissues.

The traditional experimental method is based on the study of histological cuts performed in the zone with the implanted biomaterial. This methodology implies to sacrifice several animals at several implantation times and this supposes two drawbacks: the first one is the sacrifice of unnecessary animals and the second one is that the study of the evolution of the material is performed on different animals. Moreover, the histological cuts have to be performed in one plane orientation which is selected manually and some sample material between cuts is lost in the cutting process. These drawbacks could be overcome by following the so-called in-silice experimentation.

The main goal of this work is to compare the information coming from imagery processes (in-silice experimentation) with the traditional information obtained from histological cuts.

We describe an in-silice experiment as a part of a project in which participate 3 groups: a materials group, responsible of the design and study of the biomaterials, a veterinarian group, responsible of the implantation, care and sacrifice of the animals and our computer graphics group, interested in the modelling and visualization of 3D time-varying volume datasets.

As from the project protocol we weren't able to perform in-vivo experimentation, we had performed an in-vitro experiment. We applied for an experiment to be done in the ID17 Laboratory of the ESRF (European Synchrotron Radiation Facility) in Grenoble and we were allowed to use this beam line for five days. The ID17 Bio-medical beam-line gives support to research programs involving both imaging for diagnosis and irradiation for therapy. The computed tomography facility takes place in a satellite building, located 150 m from the source point.

After the capture process, the CT reconstruction process was also applied in the ESRF and then we developed ad-hoc software and used our existing Volume Visualization Platform to obtain voxel models from the images and to perform processes as clipping, segmentation and visualization.

This paper is arranged as follows. Next section describes the methodology of the experiments realized in order to capture the images of the obtained samples together with the software performed and used to process these images. Section 3 comments the obtained results and the last section gives the conclusions and discusses future work.

2 Methodology

The whole experiment consists in the study of the evolution of four temporal sets: three (m1, m2, and m3) with a biomaterial implanted and one without any implant (control). The three materials were two cements, hydroxipatite deficient in calcium, $Ca_9(PO_4)_5(HPO_4)OH$, one dense and the other porous, and one glass, calcium phosphate reinforced with TiO_2.

The periods to study were three: at 1, 4 and 12 weeks (t1, t2, and t3, respectively). The animals used were New Zealand white rabbits 4 months old and the materials were implanted at the femoral ends. So, we were provided with 12 samples fixed in formol from which we obtained the images and which also were used after for the histological study.

The computer-assisted experimental process realized on the samples consists of two main steps: the construction of graphical models of the implants and the virtual manipulation of these models. Figures 1 and 2 show these two steps separately. The first step (see Figure 1) consists of the data capture (DC), i.e. the acquisition of a 3D stack of images of the bones. Then, 3D voxel models are constructed (MC) by separating the samples in the images, since there are three samples per image set (see Subsection 2.1), and clipping empty space. The implants are next segmented from the models (IS). Once the implant models are constructed, in the second stage of the pipeline (see Figure 2), they are aligned in the registration process and used for rendering, animation and measurements.

All the algorithms designed for this pipeline have been implemented on our Volume Visualization Platform *Hipo*. We next describe them.

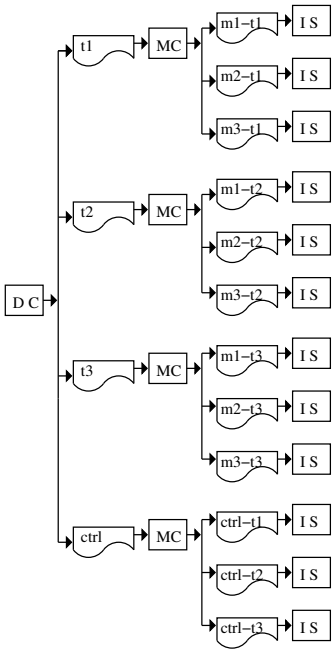

Figure 1: First three steps of the pipeline: data capture (DC); model construction (clipping and model separation) (MC); implant segmentation (IS)

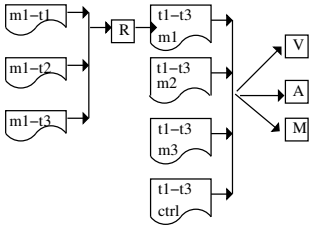

Figure 2: Second step of the pipeline: registration, measurements , rendering and animation.

2.1 Data capture

The image generation process was performed at the ESRF. In order to save beam time, we captured three samples at a time (see Figure 3). Thus, we obtained four image sets: one set of images has the control samples corresponding to the three time periods (see *ctrl* in Figure 1); the other three sets have the implant

samples at the weeks 1, 4 and 12, respectively (see *t1*, *t2* and *t3* in Figure 1). So, we have the three implant samples at the same week in the same image set. The control set shows the natural evolution of bone repair.

Figure 3: Set $t2$, i. e. the three implanted samples corresponding to 4 weeks

The precision of the capture system is $47\mu m^3/voxel$ and the sample height was about $3cm$, so we obtained more or less 800 slices, which could be processed in groups of 72. The final resulting file size was of 1929321 (1389x1389) bytes for each image. The capture system generates a synogram for each slice. After the capture, a CT reconstruction process was performed with a customized software available at the ID17 line. From each synogram, this software generates a 2D slice of voxels with floating point associated values. This was the information which came from the ESRF.

2.2 Model construction

A clipping and separation process was performed to each image set in order to obtain suitable voxel models for all the 12 samples. First of all, we merged all the 2D slices and coded the values in a byte obtaining a 3D voxelization of $1389 \times 1389 \times 772$. Since the voxelization showed a large quantity of empty space, we next clipped the volume by the minimal containing box of the three samples inside it, obtaining 3D voxelizations of about $1024 \times 1024 \times 680$.

After this, since each model contained three samples, we performed the separation process: from each image set, we extracted three voxel models: one for each sample. The separation is performed using a customized connected component labeling algorithm. This algorithm is based on three assumptions that the images fulfill: (a) the bones are composed of connected sets of voxels, (b) although close one to each other, the bones are not connected to each other, (c) the background color is clearly different from the bone pixel colors. According to this, the separation algorithm consists of computing connected sets of non-empty pixels in the volume, i.e, *connected components*.

The algorithm scans the volume slice to slice, updating a list of connected components. For each voxel of a slice with a value larger than a given threshold, we check it if belongs to the already created components. Three cases may happen: (i) the voxel does not belong to any component, therefore, a new one is created, (ii) the voxel belongs only to one component, which is consequently updated, (iii) the voxel belongs to two o more components, thus, the components are merged into one. Figures 4 and 5 show one slice of one set of three samples and one slice of one extracted sample, respectively.

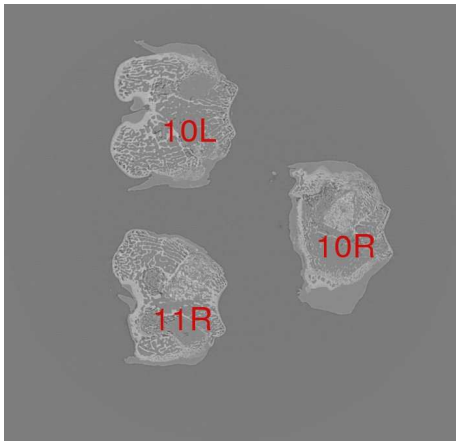

Figure 4: One slice of the set of the three samples corresponding to 4 weeks (10L = porous cement, 10R = dense cement, 11R = glass)

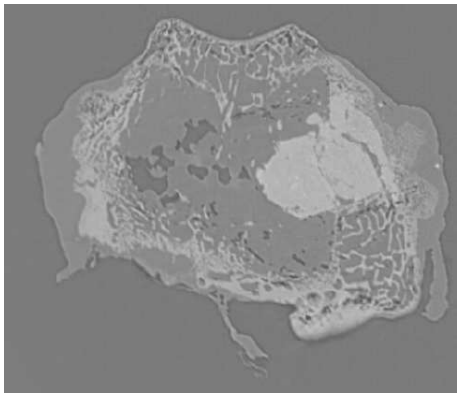

Figure 5: One slice of the sample with dense cement at 4 weeks

The brute-force implementation of this method is both memory and computationally expensive, since the connected components may be composed of a large number of voxels, and checking if a voxel belongs to a connected com-

ponent has a linear cost with number of voxels of the component. We reduce this complexity by representing the connected components as their 3D bounding box and the cross section of the connected component in the current and the previous slice (see Figure 6). The cross sections are represented as black and white images for inside and exterior voxels, respectively. The algorithm first checks if the voxel belongs to any bounding box of a connected component. If so, it checks if it is connected to the voxels of the current cross section or to the voxels of the previous cross section. Since the cross sections are represented as images, checking if a voxel is connected is a very fast traversal of an 8-connected neighborhood. The algorithm is very fast and works effectively to separate the samples.

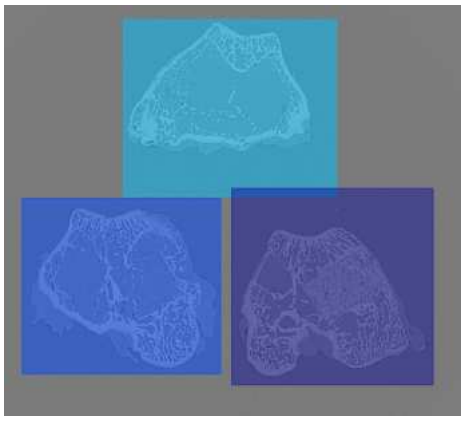

Figure 6: Bounding boxes used in the connected component labeling algorithm applied to separate the three samples

2.3 Implant segmentation

The implant segmentation was the more tedious part of the process. Several automatic and semi-automatic strategies were used, with different results depending on the type of implant. First, the models were filtered slice to slice in order to enhance edges, using the image processing library ITK [1]. Then, we designed a 2.5D region growing algorithm that, based on a seed voxel, belonging to the implant, computes the connected region of voxels whose values differ from the seed value less than a given threshold. The algorithm is 2.5D because the regions grow in 2D but the connectivity is checked in 3D with the previous and the current slice. Only voxels connected with voxels of the current slice and at least one of the previous slice are included in the region, in order to avoid elongated artifacts. This strategy works well for the dense cements which have been segmented totally automatically, but it fails for the heterogeneous structure of the porous cements, because it softens them excessively. Therefore, for the porous cements, the purely 2D region growing algorithm was applied, giving

as a result a very thorny shape, that was then refined manually by contouring.

2.4 Model manipulation

The constructed models have been rendered using a splatting algorithm [6] with emission and absorption shading [4] for interior voxels and Phong shading for boundary voxels [2]. Their surfaces have been extracted with Marching Cubes [3] and rendered using OpenGL. Finally, cross-sections of the models have been computed and compared to the histological cuts. Figure 7 shows two 3D visualizations of a sample. The models have been aligned manually in order to obtain 4D (space+time) models (see *Registr.* in Figure 2). However, the implants were not located at the same exact positions in the bones and the morphological differences between bones were too large to simulate a continuous animation process. This would require an in-vivo image capture on the same specimen.

The absorption of the Bio-implants for dense cements and glass can still be evaluated quantitatively on the samples from different animals because, initially, the implants have the same volume and, in the case of the glasses, the same cylindrical shape. Therefore, the loss of volume of each implant along time can be used as a measure of the biomaterial absorption. For dense cement and glass, the volume implant can be computed as the sum of the volume of the internal voxels and an estimation of the volume of the boundary voxels. In this paper, the contribution of a boundary voxel has been approximated as one half of the volume of a whole voxel. We plan to compute the volume more exactly, taking into account the actual occupation of the implant in the boundary voxel, using the boundary case typification of the Marching Cubes algorithm [3].

In porous cement, this volume computation strategy is not feasible, since the material is scattered through the volume. Higher resolution images would be necessary in order to count the pores and estimate their volume.

3 Results

In order to validate the in-silice experiment, we compared the cross section computed on the models with the histological cuts observed with optical microscopy and SEM (Scan Electronic Microscopy). Figure 8 shows the image (left) of one slice of the glass material at the three periods of time and the corresponding histological cuts seen with the optical (in the middle) and the electronic (right) microscopes. Figure 9 shows the three materials and control at the same instant of time, the image at left and the equivalent histological cut with optical microscopy at right. From a biological point of view, the relevant features of the images are the histomorphometrical parameters of percentage of implant re-absorption and percentage of bone tissue neoformation. Both features can be evaluated qualitatively using the three technologies. Quantitative measurements of these parameters have been performed in the in-silice protocol by computing the volume of the implant. The main advantage of these measurements is that

they are 3D, whereas in the histological cuts, these parameters are computed in 2D (area measurements) and extrapolated to 3D. However, quantitative measurements on very porous materials would require higher zooms (40x to 100x) on the histological cuts as well as in the images, because the material is scattered through the volume. Optical microscope can give this resolution, but nano scale image capture would be necessary for in-silice experiments. In this point, in-silice experiment can be used as a complementary tool to histological evaluation: it can be used to select the best plane orientation used in the histological cut later analyzed using optical microscope.

4 Conclusions and future work

In this paper, we have described an experimental process of evaluation of bone implants using 3D images. The process involves the capture of the images, the segmentation and reconstruction of the 3D models and their visualization. All the algorithms have been implemented in our Volume Visualization Platform *Hipo*. The results have been compared with those provided by histological cuts. We conclude that the in-silice experimentation can enhance and speed up the traditional laboratory experimentation. In the future, we plan to design customize software tools to better simulate the real experimental process such as virtual tinction, multiplanar cuts and more precise volume evaluation.

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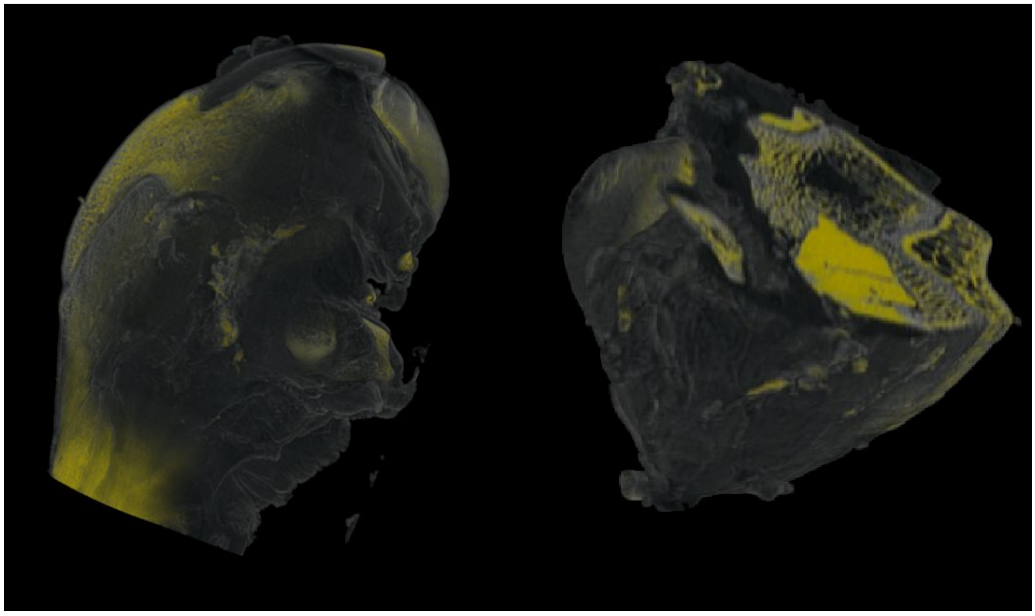

Figure 7: 3D visualization of the sample corresponding to 1 week and with dense cement: at left, the whole model and at right, the model clipped to show the material implanted

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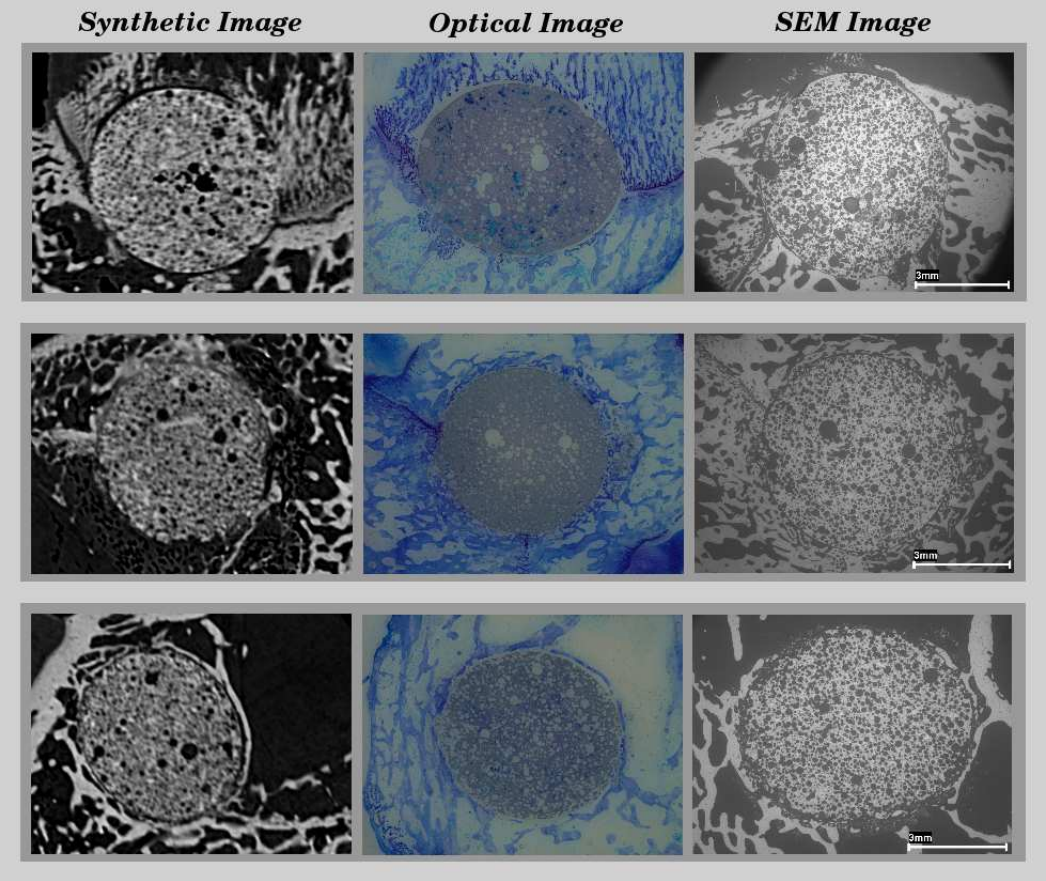

Figure 8: Image (left) of one slice of the glass material at the three periods of time and the corresponding histological cuts seen with the optical (in the middle) and the electronic (right) microscopes

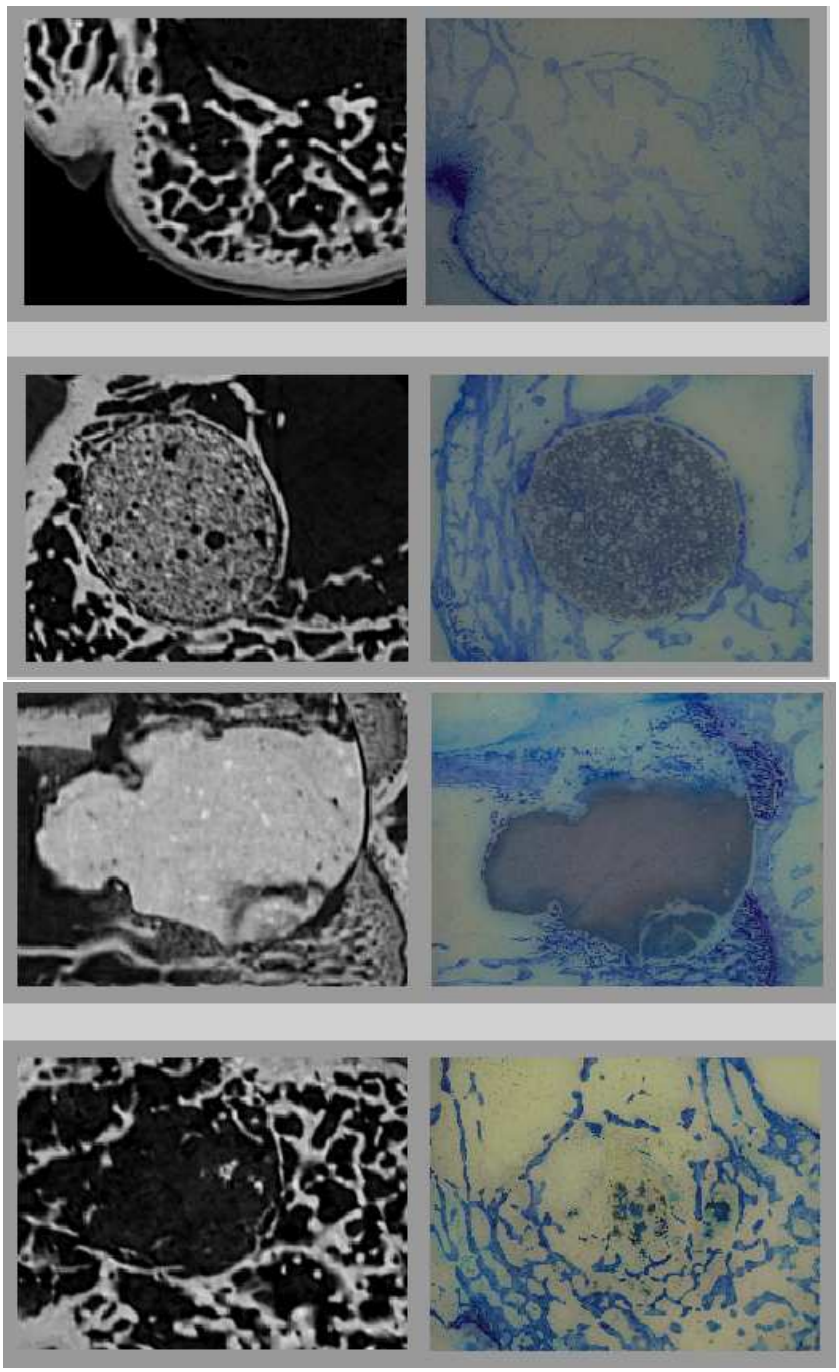

Figure 9: The four materials, from top to bottom, control, glass, cement dense and cement porous at the same instant of time, the image at left and the equivalent histological cut with optical microscopy at right