



Human skeletal system virtualization by using solid voxels models

Jorge Alonso ^(a), Rafael Álvarez ^(b), Jorge Rocas ^(b)

^(a) Universidad de Oviedo. Dpto. Ingeniería Eléctrica, Electrónica, Computadores y Sistemas. Campus de Gijón. EDO2 33203 Gijón

^(b) Universidad de Oviedo. Dpto. Construcción e Ingeniería de Fabricación

Article Information

Keywords:

K1, Biomechanics
K2, Virtual Models
K3, Voxel Models
K4, Finite Element Method
K5, Medical Imaging

Abstract

The biomechanics of the 21th century rely increasingly on virtual models of the muscle-skeletal system. Virtual bone models allow to the investigators, among other applications, to test their prosthesis designs without putting in any risk human lives.

This article describes the methodology developed by a multidisciplinary team of physicians and engineers in order to create virtual models of bones. The generated virtual models show analog mechanic properties to the living tissue and are susceptible of being manipulated by a standard program of Computer Assisted Design (CAD) which offers a wide range of possibilities.

A fully functional computing program has been implemented in order to test the methodology: modVOX. This program generates virtual voxel models in a fully automated manner. These models have been verified with standard virtual models of Finite Elements Method (FEM) demonstrating similar result to those of the models

1 Introduction

In order to assimilate the mechanical features of a human bone to a virtual model, it is necessary to start from a data source with information about them. The most versatile and non-invasive source of information about bone tissue is biomedical image. Particularly, the Computerized Axial Tomography (CAT) allows getting sections of a human body, the pixels of which have a co-relation with the density of the tissue that has been scanned [1, 2, 3].

The proposed methodology starts from a set of tomographies (**CT**) of the bone to be modeled, taken at regular intervals. Given the harmful nature of the radiation emitted by the tomography scanners, it is common to work with femurs of frozen cadavers, which keep intact the mechanical properties of the living tissue. The use of frozen bones requires lower degree of processing work, because those bones do not have any adjacent tissue.

Grosso modo, the proposed methodology uses as the only input data a series of CT (fig.1) acquired at regular intervals, covering completely the bone to be modeled. Usually, the CTs are obtained in DICOM[®] format and have to be processed in three different aspects. The first step is to remove from each tomography the pixels which do not correspond to the bone tissue. It is also necessary

to remove any object alien to the bone. Secondly, the resolution has to be adapted to the size of the model to be generated. And finally, the file format needs to be changed in order to enable its interpretation by the software to be implemented. The series of processed images will lead, through a process of interpolation, to a Master Voxel Model (**MV**m), which will be used to generate, applying statistical methods, so-called voxels submodels (**MV**). The **MV**, which can be generated in different voxel sizes, are elements which can be converted automatically into Solid Voxel Models (**VM**s) in a CAD program workspace, which supports three-dimensional models; modVOX[®] generates the MVs in AutoCAD[®], an Autodesk[®] Company software.

Nowadays the voxel models are successfully applied in different fields of biomechanics, such as simulation of surgeries [4], studies of muscle-skeletal system [5, 6, 7], and design and virtual testing of implants and surgical instruments [8].

1.1 Background

A volume element is called voxel because of its similarity with the term pixel: "the smallest homogeneous surface composing an image, defined by its brightness and color". The word comes from the contraction of the term *Volumetric Element*.

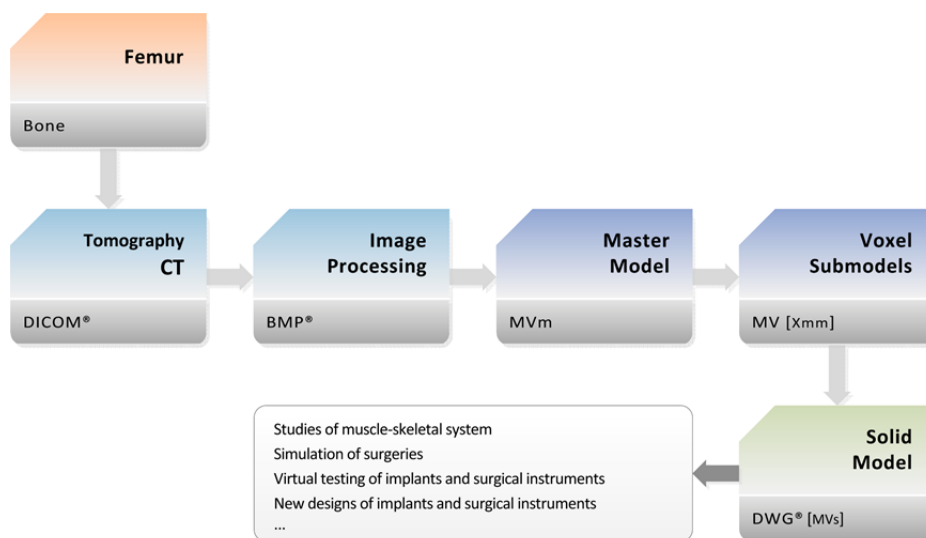


Fig. 1 Proposed methodology block diagram

In the same way as pixel stores information of light variations (brightness, color, relations between color and magnitude...), a voxel can have one or more associated magnitudes. They are usually related to the material properties, which are considered homogeneous in the volume of the voxel. For example, a voxel can have associated an average density value of a material contained in its volume (fig. 2).

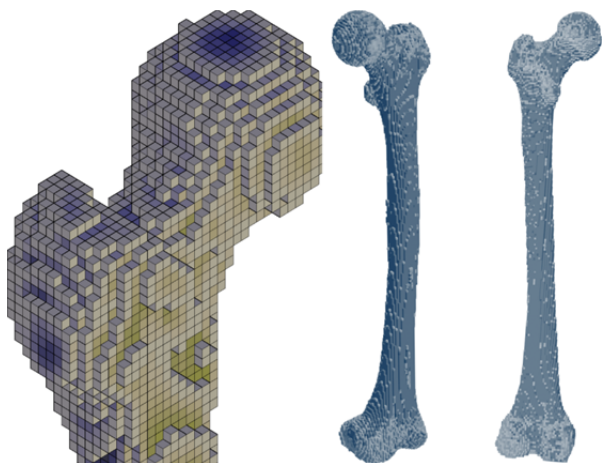


Fig. 2 Cubic voxels model of 3 millimeters of resolution

The pixels are used in bidimensional representations of objects. If the data contained in a group of pixels has light properties, it is said that the pixels compose an image. The voxels, for their part, are used in order to represent objects in three dimensions. In the frequent case, when the information contained in a set of voxels is related to physical properties of a material, it is said that the voxels represent a body (fig. 3). The pixels are rectangular elements (usually square) characterized by their individual size, which is defined by two dimensions, or by a single one, if the pixel is a square.

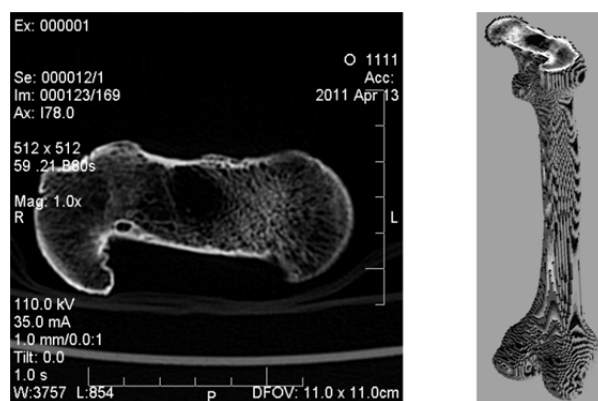


Fig. 3 Tomographic image of pixels (left) and sectioned voxels model (right)

The more pixels are used to represent an object, the more detailed is that representation. The voxels, for their part, are also characterized by their individual dimensions. In theory, they can have any polyhedral shape, which allows *geometric compactness* (compact stacking). However, in practice, there are only few applications that do not use hexahedral voxels, in which case they are characterized by three dimensions (length, width and height), or only one in they are cubic.

Since the final goal of voxels usage is to model regions of space, the term voxels model is used to describe "an ordered set of voxels, which has approximately the same volume and shape as the region of space that is intended to be modeled". Obviously, since the intention is to define with a voxels model a continuous region of space, the model should not leave unoccupied volume spaces within the complete volume that is to be modeled. A voxels model has to represent geometric compactness, in an analogue way as the pixels of an image have to completely cover the area of representation.

Both in the case of pixels and voxels, their groups (images or bodies) normally are *homogeneous*, meaning that all their components have identical shape and dimensions in order to facilitate the processing of the model. Heterogeneous models allow modulating of the objects definition which is achieved by representing them per regions. In those cases, the distribution of pixels or voxels is denser in the more complex areas of the objects that are being represented.

The groups of pixels and voxels are together quantified by their *resolution*: the number of them which can be arranged in an organized way in certain unit of area or volume. Having in mind that the individual shape of each voxel may not exactly match the shape of the exterior or interior surfaces of any type of volume, it is accepted that a voxels model is an approximate model of the represented object. The higher its resolution, the less approximate is the model (fig. 4).

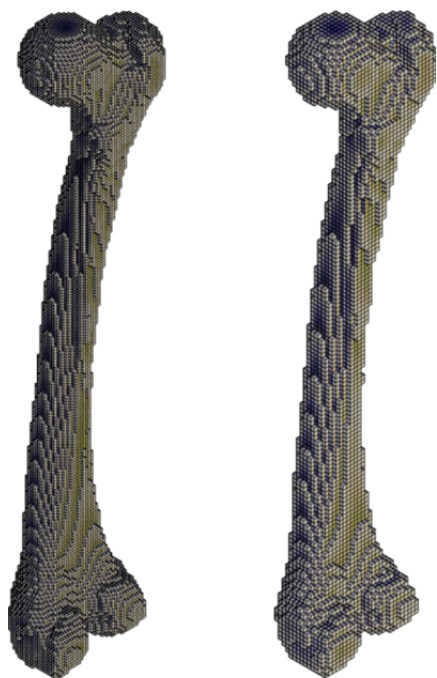


Fig. 4 Cubic voxels model of 2 mm (left) and 3 mm (right)

1.2 Voxels models vs. mesh models

The values assigned to each voxel of a model can come from different sources (experiments, mathematic models...). Another category of virtual models is formed by the so-called mesh models. In rough outlines, a mesh model consists in an approximation to the surfaces of an object made with a set of polygons connected by their edges. The greater is the number of used polygons, the better will be the achieved approximation to the modeled surface. Since a mesh approximates the surfaces of a solid, if the objective is to model an object with internal variations in its material (as in the case of a bone composed by cortical and trabecular tissues), the model should be segmented in such a way, that each part with certain material properties would be marked out by a mesh. The picture 5 shows how the density variations of the bone tissue in a human femur has been modeled using mesh modeling. An external mesh models the external surface of the femur. Another, internal one, models the hypothetical boundary between cortical and

trabecular bone. Such models can be used in order to perform mechanical studies by FEM, with which it is possible to determine the internal stresses state of the bone, among other possible Biomechanical studies [9].

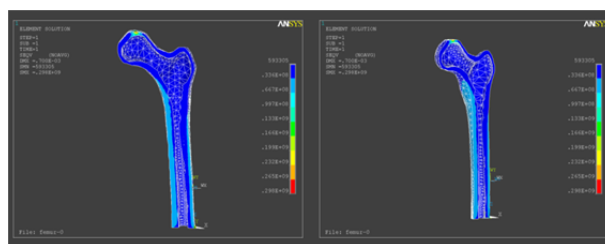


Fig. 5 Two meshes model of a femur with internal structure of the bone

To quantify properties of the bone tissue with 2 values is inaccurate. In theory, it is possible to determine more regions of the bone using meshes, which model the boundaries between areas with different mechanical properties. However, since the regions of the bone tissue with similar mechanical properties tend to be very irregular and/or disjoint, in practice, it is a complex task to model more than two internal regions of a bone. On the other hand, the voxels models allow assigning mechanical properties of a small volume of the model (voxels) to the same spatial position in which the bone material has those properties. With such information it is possible to perform virtual mechanical studies, which consider the properties associated with the volume (instead of the surfaces).

Other techniques [10, 11] allow assigning to the virtual bones models used in FEM studies, the mechanical properties of the bone tissue in each node of a tridimensional mesh, based on information from series of CT. Since the three dimensional meshes are very commonly automatically generated by the FEM software [12] it is often complicated to assign mechanical properties to the nodes from the CT. It is necessary to determine the special coordinates of each of them and the one of the closest pixel of the closest tomography of the series for each node, in order to get its corresponding mechanical property [13]. The nodes coordinates have to be determined, because, as they are generated automatically, they usually are not arranged in a regular way. Instead, hexahedral voxels models, like CT, have a similar spatial distribution, by layers. This makes the information contained in them particularly suitable to determine parameters of the voxels of the model.

1.3 Applications

Voxel models are applied in various fields of science and engineering. In biomechanics they are successfully applied in simulations of surgical interventions [14] which uses models of muscle-skeletal system, surgical instruments and implants, in order to plan, test and improve real surgical interventions, without putting at risk the life of the patients. Analogously, the voxels models of isolated bones or of a joint can be used in order to get the internal stresses states of the bone tissue [15] and their variations before the implantation of a prosthetic system [16]. This kind of studies offers information, which allows studying the behaviour of the implants "in vivo", or to improve their design without subjecting the patients to surgery.

2 Material and methods

The proposed methodology of generating the voxels models has been developed and implemented in a specific software, modVOX[®], which processes series of CT in order to generate those voxels models. The proposed method is applicable for CT of any resolution and for any equidistant separation interval between them: I_{TAC} . This variable of the methodology has to be specified before being implemented.

Due to the fact that it is relatively easy to get series of CT of equidistant sections with a separation of 1 mm or more, using a conventional hospital tomography scanner, the proposed methodology was implemented in order to process series of tomographies with this separation ($I_{TAC}=1$). In order to describe the proposed methodology and to avoid the use of variables in the notation, the case of $I_{TAC}=1$ is also considered.

The methodology is based on generating a very detailed initial voxels model, called *Voxels Master Model*, **MVm**. From this model are generated so-called *Voxels Submodels*, **MV**, which are used in the practical applications and in the experimentation. The **MVm** and the **MV** are only different in their resolution. In the implemented case, the **MVm** are cubic voxels models with 0.5 mm edge. The **MV** are also cubic voxel models, but with 1 mm edge or bigger, with 0.5 millimeters incremental size (1; 1,5; 2; 2,5... mm). The *Master Models* have been called so because they derive from the data. The so-called Submodels derive from the Master Model.

2.1 Voxels Master Models

In the proposed methodology, the CT have to be processed in order to adapt the size of the pixels to the voxels size of the **MVm**. Only in the case when that the pixels size is $I_{TAC}/2$, it is not necessary to process them. This particular implementation, described in this study, considers CT series of 110x110 millimeters and 215x215 pixels.

Due to the interval between CT, I_{TAC} , the only hexahedral voxel possible size, without modifying the number of CT of the set, is 1 mm. The resolution of the CT available for the tests was of 4,6545 pixels/mm (0,2148 mm/pixel). This implies that in theory it will be necessary to average out the brightness of 21.6644 pixels in order to determine the value of each voxel of the model of 1 mm. The value associated to each voxel will be derived from the corresponding pixel from only one tomography of the series. Due to the fact that the possibility to disregard CT of the original series, in order to generate the models of voxel size bigger than 1 millimeter, is not considered, the initial model (*Master Model*) will serve as a basis to get different resolutions models (lower).

The basic technique to generate voxels models disregards a part of the data information, because it requires more than 21 pixels to get an average brightness representation of a single voxel. That is the reason why an improvement of the basic proposed technique was developed. It consists in generating a couple of voxels between each corresponding couple of pixels of each pair of CT of one series. That way each cubic voxel will have 0,5 millimeters edge. Its associated brightness will be obtained from a lineal interpolation between the brightness of the pixels which correspond to the pair of

CT that delimitate it. It is a quarter of the previous number of pixels. Having in mind, that 2 voxels will be generated between each pair of CT, the new proposed method is able of generating 8 voxels, where before only 1 was generated. This means a lower averaging than with the data that generate each voxel (fig. 6)

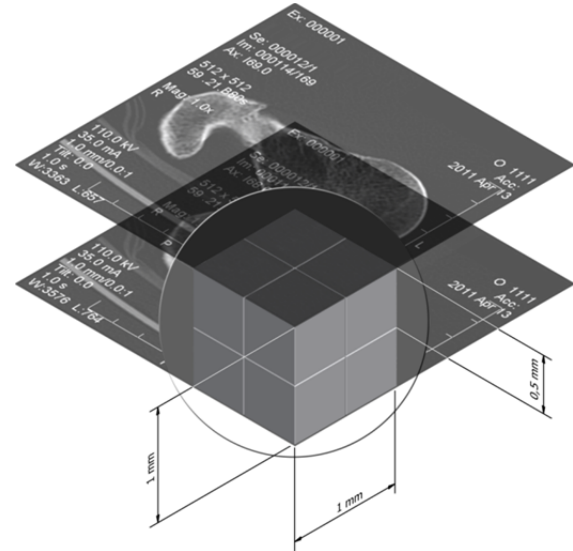


Fig. 6 Diagram of the interpolative method used in order to generate **MVm**

As far as the data structures of the voxels models are concerned, they were implemented as three-dimensional matrices of (i,j,k) indexes, which store the brightness value assigned to each voxel. The data are stored as IEEE floating comma numbers of 32 bits (4 bytes). The matrix indices i and j are considered in the plan of the CT, i horizontal and j vertical one, while the index k is considered in a perpendicular direction to the previous ones –positive in the order in which the series of CT are processed. The value associated to each voxel can be fractional, because it is obtained by interpolation.

The brightness assigned to the upper and lower voxels, respectively $B_{vm}[i,j,k]$ and $B_{vm}[i,j,k+1]$ and considering $K=1,3,5,\dots$, is determined by the brightness of the two pixels, which correspond to each pair of CT, $B_p[i,j,(K+1)/2]$ and $B_p[i,j,(K+3)/2]$, according to the following relations:

$$B_{vm}[i,j,k] = B_p[i,j,(K+1)/2] + \frac{B_p[i,j,(K+3)/2] - B_p[i,j,(K+1)/2]}{4} \quad [1]$$

$$B_{vm}[i,j,k+1] = B_p[i,j,(K+1)/2] + \frac{3 \cdot (B_p[i,j,(K+3)/2] - B_p[i,j,(K+1)/2])}{4} \quad [2]$$

It is necessary to mention that the possibility of using a lower number of pixels between each pair of CT to obtain more voxels from the *Master Model* was rejected. This was due to the fact that the interpolation index would not be 1 to 1. Thus, if pixels of 0.2 millimeters are considered, the brightness of 5 voxels between each pair of pixels has to be interpolated. To count with a *Master Model*, composed by voxels of 0.5 millimeters allows generating *Submodels* in a wider range than if departing from a model of 1 millimeter. Thus it will be possible to generate *Submodels* with voxel sizes from 1 millimeter (the value chosen for I_{TAC}) and which voxel size is increased by 0.5

millimeters. Therefore, generalizing for a sequence of $n=1,2,\dots$ will be obtained *Submodels* with voxel sizes T_{VOX} :

$$T_{VOX} = n \cdot \frac{I_{TAC}}{2} \quad [3]$$

In order to get the series of CT which generate a **MVm** composed by voxels of 0.5 millimeters, the series of images have to undergo a process which makes its pixel size of 0.5 millimeters as well, $I_{TAC}/2$. It is assumed that such a transformation of shading between images (a reduction of the effective number of pixels of the images) will not mean to introduce noise in the data. The original series of CT used in this investigation are composed of images with a resolution of 4.654 pixels/millimeter. In order for the images (of the used series for generating a **MVm**) to have pixels of 0.5 millimeters, their size has to be reduced from 512x512 to 220x220 pixels. The digital processing of the CT was performed with the Adobe® company Photoshop® 12.0 software. The images have been resampled by using a bicubic interpolation.

2.2 Voxels Submodels

The proposed methodology generates the **MV** from a **MVm** by a simple statistical method which considers the brightness of all the voxels of the **MVm**. The brightness $B_V(i,j,k)$ of each voxel of the **MV** with voxel size T_{VOX} , is obtained by calculating the arithmetic average of the brightness of the voxels of the master model $B_{Vm}(I,J,K)$ with size T_{Vm} . The considered number of voxels of the **MVm** has to be an integer multiple of the voxels size of that model. This condition will always follow the established relation (3). Therefore, there will be the following general expression for the brightness of the voxels of the **MV**:

$$B_V[i,j,k] = \sum_{\substack{I=i \\ J=j \\ K=k}}^{I=i+(T_{VOX}/T_{Vm})-1 \\ J=j+(T_{VOX}/T_{Vm})-1 \\ K=k+(T_{VOX}/T_{Vm})-1} \frac{B_{Vm}[I,J,K]}{\left(\frac{T_{VOX}}{T_{Vm}}\right)^3} \quad [4]$$

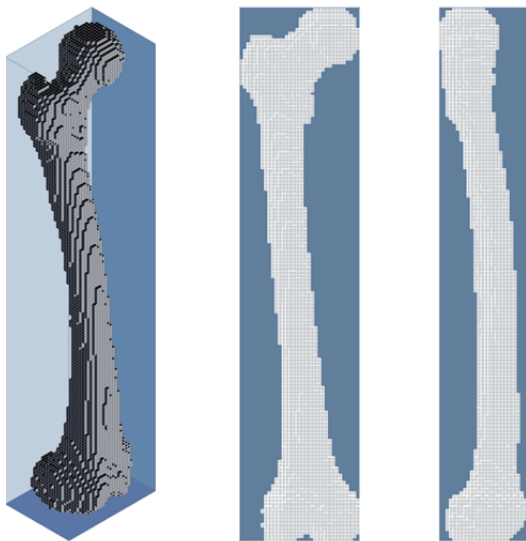


Fig. 7 Bounding Box of a MV (perspective and vertical views)

Due to the fact that the size of the data matrixes of the voxels models was optimized in order not to store null brightness, which are out of the range of the model, it can be considered that the maximum and minimum indices of the matrix **MVm** and **MV** define the *Bounding Box* of the voxels models (fig. 7). In the same way, when a series of CT is processed in order to generate a **MVm**, the *Bounding Rectangle* of the series is determined previously. *Bounding Rectangle* is the smallest rectangle which can contain all the pixels of non-null brightness of all the CT of one series (fig. 8).

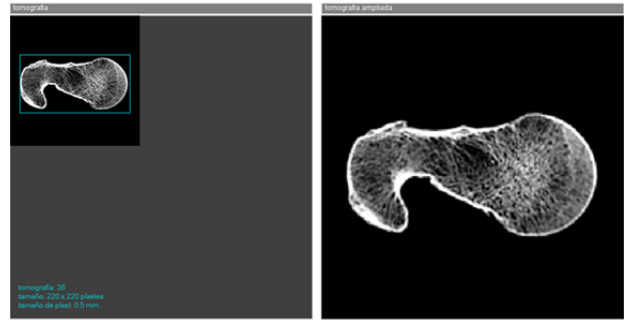


Fig. 8 Bounding Rectangle of a series of CATs (left)

2.3 Solid Voxel Models

The data files that contain the **MVm** and **MV** information are numerical files that store the average brightness value assigned to each voxel, **MVm** (i,j,k) and **MV** (i,j,k) together with some information associated with the model. However, in many biomechanical studies with voxels models it is desirable to have them in a more versatile format. Nowadays, a large part of those studies are conducted using three-dimensional CAD software. In the literature of reference those techniques are called bio-CAD [17]. The methodology proposed in this study includes a final phase which generates, in an automatic manner, solids models, **MVs** of the generated voxels models. Those models can be manipulated identically to a solids model created with appropriate software (such as a model of a surgical implant).

Each voxel of the generated **MVs** are Right Prism (a kind of geometric objects). They are defined by the three-dimensional coordinates of one of its vertex and by their three dimensions. Each prism which models the voxels of the **MVs** is an independent object and is associated with a unique layer which identifies its range of bone density. Thus, the voxel with a brightness of **MV**(i,j,k) is associated with a layer with name:

$$\text{MAT-Dmed-[Dini-Dfin]} \quad [5]$$

where **Dmed** is the average density of the densities range of the voxels associated with the layer and **Dini** and **Dfin** are the extreme values of that range.

The properties of the bone tissue were assigned to the **MVs** by applying the empirical relations between the Hounsfield units (HU), the density (ρ_{TAC} , g/cm³) and the elastic module of the material (E , MPa), as well as the values used in the bibliography for the average densities of the cortical and trabecular bones, according to the studies of [18, 19]. Due to the fact that it is not possible to

count with an unlimited number of layers, in order to assign the voxels of the solids model including the whole range of covered densities, it was decided, for the implementation, to count with between 1 and 100 ranges of voxels density values. This implies that the final model will have between 1 and 100 layers. For each range of density is considered its average value as the effective density of the materials of each voxel.

In order to create the **MVs** automatically, Autodesk® company software AutoCAD® was used. That software allows automating its functions by the use of the ActiveX® technology by Microsoft®. The proposed methodology creates a prism object located in a spatial position, which corresponds to the coordinates of the indices of each voxel, **MV**(i,j,k), considering the voxels size of the model. A layer of AutoCAD® is created automatically for each range of densities of the bone material, to which will be assigned the corresponding voxels (fig. 9). If it is necessary to work with the information of the material assigned to each AutoCAD® layer, it will be necessary to consider the name that is automatically assigned by modVOX® (5). In order to make it possible, it is simply required to consider the parameters which record (the average density and the range of densities of the material associated to the layer) or to develop an specific software capable to work with that information.

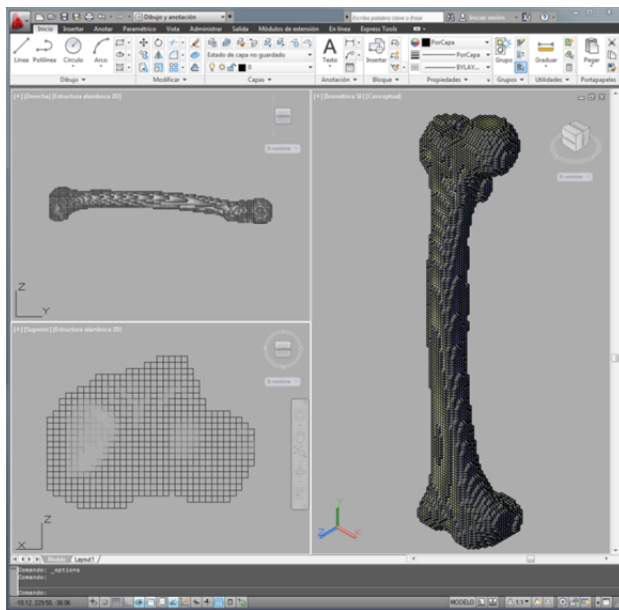


Fig. 9 MVs of 3 mm generated with AutoCAD®

2.4 modVOX® software

The implementation of the proposed methodology, considering $I_{TAC}=1$, has been performed with modVOX® software which is executed in Microsoft® operative systems. In order to generate the **MVs** it is necessary to have installed the AutoCAD® software with which modVOX® interacts.

The software allows to process series of CT stored in grey scale of 8 bits per pixel and in Bitmap BMP® format (fig. 10), to create **MVm** from a series of CT (fig. 11), create **MV** (fig. 12) and to create **MVs** from a **MV** (fig. 13).

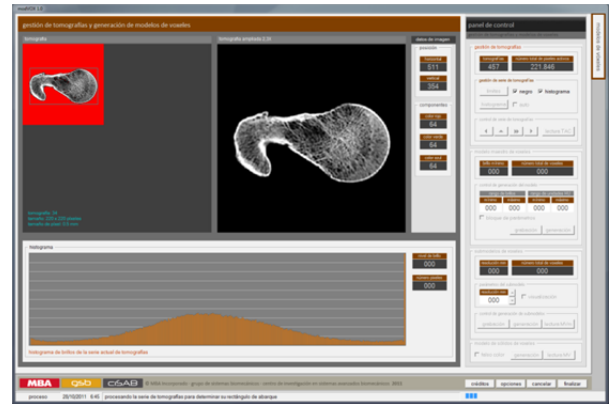


Fig. 10 modVOX® interface processing a series of TACs

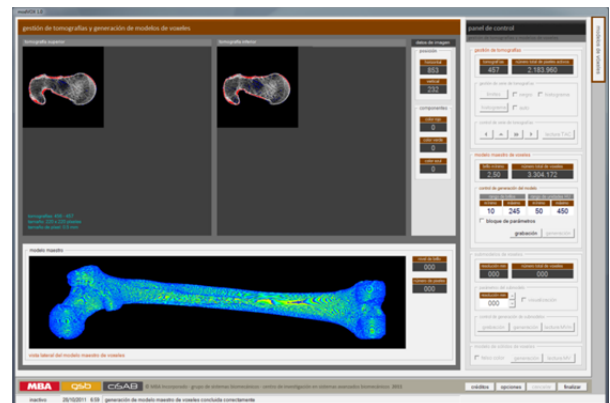


Fig. 11 modVOX® interface generating a MVm

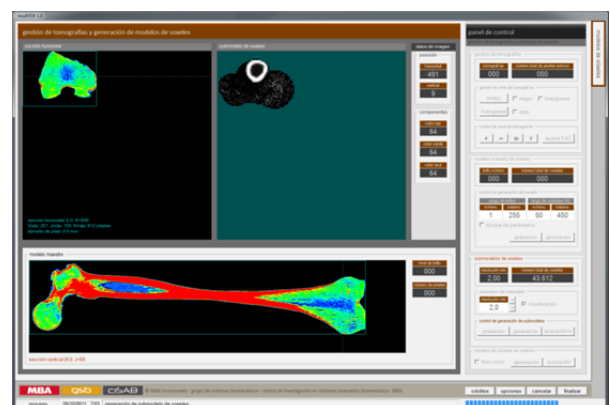


Fig. 12 modVOX® software generating a MV

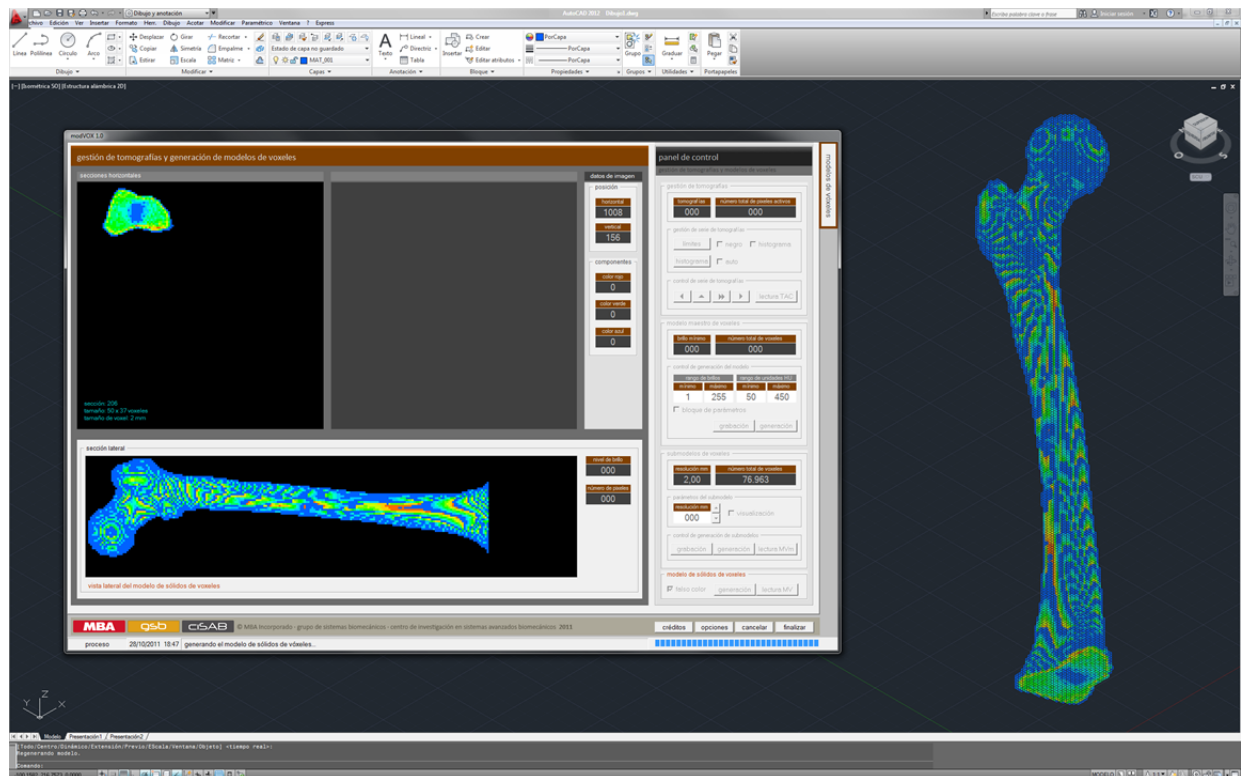


Fig. 13 Creation of a MVs in AutoCAD® with modVOX®

3 Results and Conclusions

In order to validate the methodology developed for a generation of voxel models, a comparative study between two internal stresses states of two virtual models of the same femur was performed, a standard mesh model (MME) [13] and a voxels model (MV) loaded and subjected to the same contour conditions [20]. The results were compared in seven control locations, considering that a good correlation between the internal stresses values of the femur in those regions will be accepted as a test in order to validate the model.

The data of the used MME come from the same set of CT, which have been used also to generate the MVs to be validated. In order to generate a MME the methodology described by [21, 22] was followed. The result is a tri-dimensional mesh with quadratic tetrahedral elements of 10 nodes (solid92) by the automatic meshing of ANSYS® v.12. Meshing was performed of the surfaces model generated from the same set of CT with which was generated the MVs to be validated [23].

The properties relative to the material of the MME were assigned in an analogous manner to the MVs. In accordance with [24, 25], three states of load, representative of daily activities were considered: an intermediate phase of walking (EC_1) and extreme situations of abduction (EC_2) and adduction (EC_3). The table 1 shows the loads and the angles applied for the 3 situations.

The models to be compared were analyzed by FEM in order to determine their internal stress states. In order to perform that study, the MVs has been automatically meshed with hexahedral elements of 8 nodes (solid45), assigning it material properties from the modVOX® generated data. According to Tsubota [26], for the most of biomechanical studies it is sufficient to consider the stresses in a coronal plane, therefore a comparative study considering points of the bone tissue in that plane was performed. In order to avoid the FEM models nodes interpolation, identical pairs of Von Mises images were used (regarding position, size and resolution) for each of the studied cases (fig. 14).

State	Description	F_{ART} [kN]	A_{ART} [°]	F_{TRO} [kN]	A_{TRO} [°]
EC_1	Intermediate phase of walking	2,317	24	0,703	28
EC_2	Extreme situations of abduction	1,158	-15	0,351	-8
EC_3	Extreme situations of adduction	1,548	56	0,468	35

Tab. 1 Applied loads to the considered virtual models for each phase of walking

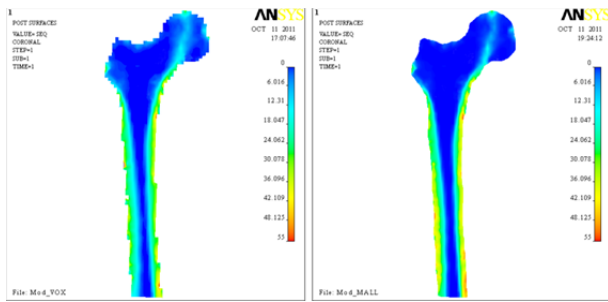


Fig. 14 FEM analysis of a MVs (left) and of its homologous MME (right) · Loads state EC₁

They were defined the regions of control by seven points, $P_{C(i,j)}$, located in the images of the FEM analisys of the **MME** (fig. 15). The comparison points have been elected based in its anatomic relevance [27]: 3 points in the approximated section of the proximal edge of the isthmus (d_{BPI}). P_{C1} in the center of the medullar channel. P_{C2} and P_{C3} in the approximated center of the corresponding sections of cortical bone. Two points P_{C4} y P_{C5} , in two locations of the center of the medullar channel, P_{C4} in the center of the channel at the height of the lower trochanter region and P_{C5} at the height of the distal heigh of the isthmus (d_{BDI}). A point , P_{C6} in the lower trochanteric región, and another one in the section of the femoral head inside the region of transmission of loads to the joint, P_{C7} .

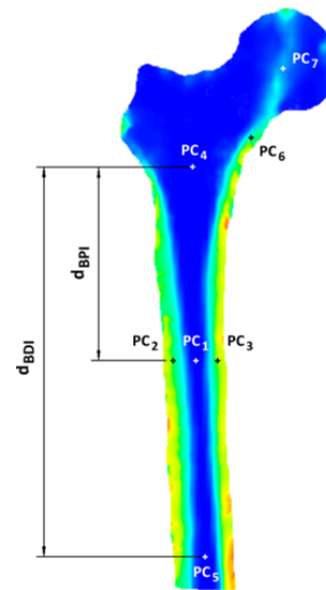


Fig. 15 Internal stresses comparison points

The results obtained have been collected in the table 2. They are been provided the values of the internal stress in MPa of the **MME** y del **MVs** for the seven points of comparison and the 3 load states. It is been indicated the absolute and relative variation with respect the **MME**.

			Points of comparison						
Load states			PC ₁	PC ₂	PC ₃	PC ₄	PC ₅	PC ₆	PC ₇
STATE 1	EC ₁ (MESH) [Mpa]		0,000	36,094	37,383	1,289	0,000	24,922	10,957
	EC ₁ (VOXELS) [Mpa]		0,000	37,598	36,309	1,504	0,000	23,203	12,461
	Variation	Total [Mpa]	0,000	1,504	-1,074	0,215	0,000	-1,719	1,504
		Percentage	0,0%	4,2%	2,9%	16,7%	0,0%	6,9%	13,7%
STATE 2	EC ₂ (MESH) [Mpa]		0,000	17,188	18,262	0,859	0,000	11,816	5,156
	EC ₂ (VOXELS) [Mpa]		0,000	18,262	17,402	1,074	0,000	10,742	6,230
	Variation	Total [Mpa]	0,000	1,074	-0,859	0,215	0,000	-1,074	1,074
		Percentage	0,0%	6,3%	4,7%	25,0%	0,0%	9,1%	20,8%
STATE 3	EC ₃ (MESH) [Mpa]		0,000	22,988	23,418	0,859	0,000	16,113	6,875
	EC ₃ (VOXELS) [Mpa]		0,000	24,277	22,129	0,859	0,000	13,750	8,594
	Variation	Total [Mpa]	0,000	1,289	-1,289	0,000	0,000	-2,363	1,719
		Percentage	0,0%	5,6%	5,5%	0,0%	0,0%	14,7%	25,0%

Tab. 2 Internal stresses of the load states considered

As it can be appreciated in the graphics of linear regression in the figure 16, the average correlation coefficient of the **MVs** and the **MME** has a value of 98.9% with an average gradient of 0.98. Taking into account that the proposed methodology allows to obtain automatically the voxels model, instead of facing a tedious work what it

is usually a manual work for generating the mesh model (which uses to come from a set of CT). Due to that, it can be concluded that the proposed methodology offers evident advantages in order to perform biomechanical studies related with the internal stress state of the bone tissue.

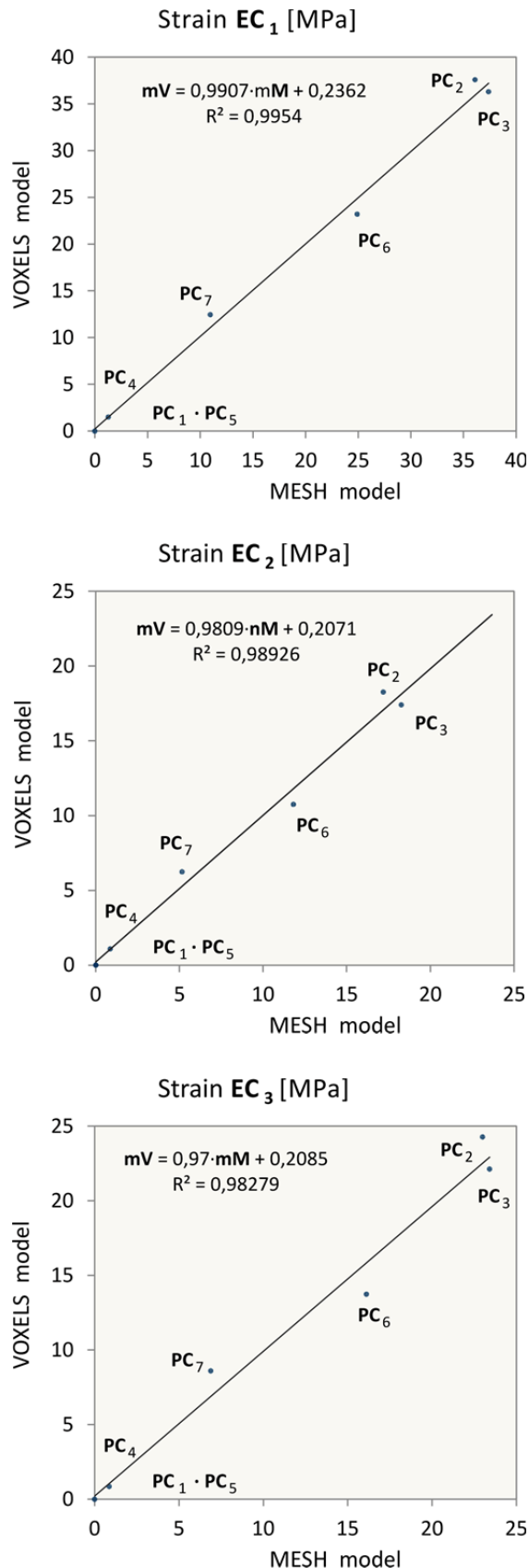


Fig. 16 Linear regression graphics

4 Acknowledgements

This work was funded by the medical services company MBA Incorporado S.L. in the context of the investigation project with the University of Oviedo called “*Technology for the non-invasive study and postoperative follow-up, of the knee arthroplasty*”.

References

- [1] S.C. Cowin. Bone Mechanics Handbook. Boca Raton. CRC Press, 2001. ISBN: 0-8493-9117-2
- [2] D.L. Kopperdahl, E.F. Morgan, T.M. Keaveny. Quantitative computed tomography estimates of the mechanical properties of human vertebral trabecular bone. Journal of Orthopaedic Research. 20-4 (2002) pp 801-805
- [3] C. Zannoni, R. Mantovani, M. Viceconti. *Material properties assignment to finite element models of bone structures: a new method*. Medical Engineering & Physics. 20 (1998) pp 735-40
- [4] Z. Yosibash, N. Trabelsi, C. Milgrom. Reliable simulations of the human proximal femur by high-order finite element analysis validated by experimental observations. Journal of Biomechanics. 40 (2007) pp 3688-3699
- [5] C. Boyle and I.Y. Kim. Three-dimensional micro-level computational study of Wolff's law via trabecular bone remodeling in the human proximal femur using design space topology optimization. Journal of Biomechanics. 44 (2011) pp 935-942
- [6] I.J. Jang, I.Y. Kim. Computational study of Wolff's law with trabecular architecture in the human proximal femur using topology optimization. Journal of Biomechanics. 41 (2008) pp 2353-2361
- [7] J.H. Keyak, S.A. Rossi, K.A. Jones, et al. *Prediction of fracture location in the proximal femur using finite element models*. Medical Engineering & Physics. 23 (2001) pp 657-664
- [8] G.J. Jense. *Voxel-based methods for CAD*. Computer-Aided Design. 21-8 (1989) pp 528-533
- [9] P.J. Prendergast. Finite element models in tissue mechanics and orthopaedic implant design. Clinical Biomechanics. 12-6 (1997) pp 343-366
- [10] F. Taddei, A. Pancanti, M. Viceconti. An improved method for the automatic mapping of computed tomography numbers onto finite element models. Medical Engineering & Physics. 26 (2004) pp 61-69
- [11] M. Viceconti, M. Davinelli, F. Taddei, et al. Automatic generation of accurate subject-specific bone finite element models to be used in clinical studies. Journal of Biomechanics. 37 (2004) pp 1597-1605

- [12] M. Viceconti, L. Bellingeri, L. Cristofolini, et al. *A comparative study on different methods of automatic mesh generation of human femurs*. Medical Engineering & Physics. 20 (1998) pp 1-10
- [13] U.V. Pise, A.D. Bhatt, R.K. Srivastava, et al. *A B-spline based heterogeneous modeling and analysis of proximal femur with graded element*. Journal of Biomechanics. 42 (2009) pp 1981-1988
- [14] T. Takimoto, N. Suzuki, A. Hattori, et al. *Development of an elastic organ model containing voxel information*. International Congress Series. 1268 (2004) pp 395-400
- [15] P. McDonnell, N. Harrison, M.A.K. Liebschner, et al. *Simulation of vertebral trabecular bone loss using voxel finite element analysis*. Journal of Biomechanics. 42 (2009) pp 2789-2796
- [16] R. Huiskes, H. Weinans and M. Dalstra. *Adapative Bone Remodeling and Biomechanical Design Considerations*. Orthopedics. 12-9 (1989) pp 1255-1267
- [17] W. Sun, B. Starly, J. Nam, et al. *Bio-CAD modeling and its applications in computer-aided tissue engineering*. Computer-Aided Design. 37 (2005) pp 1097-1114
- [18] D.R. Carter, W.C. Hayes. *The compressive behavior of bone as a two-phase porous structure*. Journal of Bone & Joint Surgery. 59 (1977) pp 954-962
- [19] J.Y. Rho, M.C. Hobatho, R.B. Ashman. *Relations of mechanical properties to density and CT numbers in human bone*. Medical Engineering & Physics. 17-5 (1995) pp 347-355
- [20] M. Lengersfeld, J. Schmitt, P. Alter, et al. *Comparison of geometry-based and CT voxel-based finite element modelling and experimental validation*. Medical Engineering & Physics. 20 (1998) pp 515-522
- [21] C. Provatidis, C. Vossou and I.N. Koukoulis. *Investigation of the influence of mesh quality and number of materials used to simulate osteoporosis in finite element models of vertebrae*. 1st EpsMSO. Athens, 2005.
- [22] C. Provatidis, C. Vossou, E. Petropoulou, et al. *A finite element analysis of a T12 vertebra in two consecutive examinations to evaluate the progress of osteoporosis*. Medical Engineering & Physics. 31 (2009) pp 632-641
- [23] N. Trabelsi, Z. Yosibash, C. Wutte, et al. *Patient-specific finite element analysis of the human femur -A double-blinded biomechanical validation*. Journal of Biomechanics. 44 (2011) pp 1666-1672
- [24] G.S. Beaupré, T.E. Orr and D.R. Carter. *An approach for time dependent bone modeling and remodeling-application: a preliminary remodeling simulation*. Journal of Orthopaedic Research. 8-5 (1990) pp 662-670
- [25] D.R. Carter and G.S. Beaupré. *Skeletal Function and Form - Mechanobiology of Skeletal Development, Aging and Regeneration*. Cambridge. Cambridge University Press, 2007. ISBN: 978-0-521-71475-4
- [26] K. Tsubota, Y. Suzuki, T. Yamada, et al. *Computer simulation of trabecular remodeling in human proximal femur using large-scale voxel FE models: Approach to understanding Wolff's law*. Journal of Biomechanics. 42 (2009) pp 1088-1094
- [27] P.C. Noble, J.W. Alexander, L.J. Lindahl, et al. *The anatomic basis of femoral component design*. Clinical Orthopaedics and Related Research. 235 (1988) pp148-165