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TECHNICAL ANALYSIS OF HUMAN MANDIBLES

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Glossary of Latin medical terms

Cancellous = trabecular = less dense, spongy bone

Condyle = a round prominence at the end of a bone, most often part of a joint

Cortical = compact, harder, more dense bone and bone covering

in vitro = 'in glass', biological, chemical tests in laboratory test tube or Petri dish

in vivo = 'in life', biological, chemical behavior in living creatures

Mandible = jawbone, lower jaw

Maxilla = upper jaw, underside of skull

Ramus = flat, vertical spar at each end of the mandible

Symphysis = a region where two bones have fused

Trabecula (singular), Trabeculae (plural) = cavities or pores within spongy bone

Trabecular = cancellous = less dense, spongy or spongy bone

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Teljes emberi állkapocscsontok elemzése képalkotó technikával

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Dolgozatomban áttekintem az emberi állkapocscsont felépítésével, terheléseivel és anyagtulajdonságaival kapcsolatos publikációkat. Nemzetközi szinten kiemelt figyelmet fordítanak a kutatók az állkapocscsontokhoz kötődő kísérletekre, vizsgálatokra, különös tekintettel a fogimplantológiai célokra. Több cikkben méri az állkapocscsont bizonyos részegységeinek jellemző méreteit és ezek alapján vonnak le következtetéseket a terhelhetőségre [1], míg mások mandibula metszeteken végeztek mechanikai vizsgálatokat és ezeket terjesztik ki a teljes csonttra [2]. Rendkívül kevés az olyan publikáció, amelyben a teljes mandibulát elemzik.

A Budapesti Műszaki és Gazdaságtudományi Egyetem Anyagtudomány és Technológia Tanszékén több, mint 12 éve foglalkoznak aktívan orvostechnikai eszközök vizsgálatával és fejlesztésével. Éppen ezért a tanszéken kialakult tapasztalatok jó kiinduló alapot adtak kutatásaimhoz. Célom, hogy nagy felbontású CT (YXILON Y.CT Modular) felvételek segítségével részletes elemzést készítssek egy állkapocscsont topográfiájáról. Az általam vizsgált állkapocscsont humán kadaverekből származnak. A vizsgálattal meghatározom a teljes mandibulában található csontállomány mennyiségét, a mandibula teljes térfogatát. Jelenleg 1 db mandibula áll rendelkezésemre és ezen végeztem el az elemzéseket. A rétegfelvételeket 0,1 mm-enként készítettem X, Y és Z irányban haladva egyaránt. Az így létrejött képeket, megközelítően 3×500 darabot mandibulánként, egy szoftver segítségével elemeztem azok szűrkeségi szintje alapján. A program a szűrkeségi szint alapján elkülönítette a csontos állományt a lágy szövetektől. Ezzel ismertté válik, hogy a teljes csontállomány hány százaléka effektív tartószerkezet és mennyi, amely nem vesz részt a teherviselésben.

A későbbiekben ezt a vizsgálatot számos mintán megismételve statisztikai következtetések vonhatóak le, ami alapján meghatározható például a terhelhető csontállomány mennyisége az életkor és a nem függvényében. Ez az információ alapjaiban befolyásolhatja a beültetendő implantátum geometriáját és az implantációs stratégiát. Ezen felül a megszerzett ismeretek birtokában a csontpótlási módszerek alapjainak kidolgozása is megvalósulhat.

Irodalom:

1. C.L. Schwartz-Dabney, P.C. Dechow 'Edentulation Alters Material Properties of Cortical Bone in the Human Mandible' J DENT RES, September 2002; vol. 81, 9: pp. 613-617.
2. Carl E. Misch, Zhimin Qu 'Mechanical properties of trabecular bone in the human mandible: Implications for dental implant treatment planning and surgical placement' Journal of Oral and Maxillofacial Surgery, Volume 57, Issue 6, Pages 700-70

Investigation of intact human mandibles by imaging technique

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In this study I look at publications touching on the construction, load-bearing, and material characteristics of human mandibles. At the international level, the researchers pay particular attention to the mandible related experiments and investigations, particularly for dental implantation purposes. In many articles typical values of certain finite elements of jaw bones are measured and on the basis of these, deductions are made for load-bearing strength [1], while others perform mechanical tests on cross-sections of mandible and extrapolate these to the whole bone [2]. Publications which analyse the intact mandible are extremely rare.

The Department of Materials Science and Engineering at the Budapest University of Technology and Economics has for more than 12 years been actively involved with the testing and development of medical equipment. Precisely because of this, the accumulated experience of the department made a good starting point for my research. I set myself the goal of preparing, with the help of a high resolution CT scan (YXILON Y.CT Modular), a detailed analysis of the topography of a mandible. The jaw bone studied in this way was obtained from human cadavers. With this test I define the quantity of bone mass found in the entire mandible compared to the total bone volume. Currently 1 mandible has been obtained and with this I completed this analysis. I scanned the bone in layers at 0.1 mm intervals. This procedure was repeated in three orthogonal directions, x, y, and z. The pictures thus obtained, 3 times 500 images per mandible, were analysed using software on the basis of their greyness levels. By means of greyness levels the program distinguished bone mass from soft tissues. With this it was possible to establish which percentage of total bone mass was structurally effective and which took no part in load bearing.

In the near future this proof-of-process test will be repeated on a large number of samples and the statistical results promise to yield for example bone-mass quantities related to patients' age and sex. Information obtained on this basis might influence the geometry of implants and typical implantation strategies. In addition to this, knowledge amassed from this data could be the basis for the development of bone-substitution methods.

References:

1. C.L. Schwartz-Dabney, P.C. Dechow 'Edentulation Alters Material Properties of Cortical Bone in the Human Mandible' J DENT RES, September 2002; vol. 81, 9: pp. 613-617.
2. Carl E. Misch, Zhimin Qu 'Mechanical properties of trabecular bone in the human mandible: Implications for dental implant treatment planning and surgical placement' Journal of Oral and Maxillofacial Surgery, Volume 57, Issue 6, Pages 700-70

1 Introduction

Characteristics of bone in the human body have important clinical consequences, and a worldwide community of researchers working in the borderland between materials science and medical anatomy have been working for over twenty years to achieve two main goals. These are: to better understand and model the material properties of bone, and to find ways to measure the bone of human patients in vivo with metrics that capture these properties.

The driving force behind all this research has been implantology. Aside from major areas of medical implantation into soft tissue, such as arterial stent research, implants that replace or attach to bone make up a field of international interest. Be it into vertebrae, the oral cavity, or the hip joint, surgeons inserting implants into hard, skeletal body parts all need to closely understand the mechanical properties of dense cortical bone and spongy trabecular bone. Implanting replacements for bone, whether of metal or other materials, created a need for better modelling of human bone properties so as to match implants to patients' bodies with minimal mechanical strain and optimal implant survival.

Three mainly Japanese teams have worked in a range of research areas surrounding bone material properties. A team led by Katsumata looked at properties of scanners when used for maxillofacial imaging. They studied the effects of tissues outside the scan volume for cone-beam computed tomography (CBCT) in sometimes causing inaccurate density values within the area of interest. Meanwhile Kaki and colleagues did a study of mineralized cortical 3D distributions in asymmetrical mandibles using quantitative computed tomography (QCT). Uchimaya et al, investigating vertebrae, found moderately strong correlation between bone-mineral density (BMD) and no correlation between structural complexity and elastic modulus, suggesting the lack of a simple metric that varies reliably with other properties.

Several individual Turks and Turkish researchers have also been closely involved in the field. On the clinical side Turkyilmaz and colleagues checked correlations between bone density, insertion torque and dental implant stability, and Bayraktar together with Keaveny worked on theory-refinement by testing high-resolution finite-element models against bone specimens. Bilhan, Arat, and Geckli meanwhile found important inconsistencies between assessments of bone-sample density by macroscopic inspection and predictions of density of the same bone from CT scan data.

Similar doubts as to the reliability of CT scan data for judging bone density came from the Belgian team Stoppie, Pattijn, and colleagues. Taking Hounsfield numbers from a CT scan of mandible bone samples they compared these to e-modulus values derived from compression tests on the same samples, and also bone-mineral-density (BMD) results from dual-energy X-ray absorptiometry. They

found that the predictive power of Hounsfield units dropped significantly with increasing thickness of cortical bone layers on the surface of bone parts under study.

Previous work in the Department of Materials Science at the Budapest University of Technology and Economics has an international reputation in the design of implants destined for insertion into soft tissue and is also developing a profile in the mathematical modelling of hard tissue. This creates a natural niche for more clinically-oriented work on in vivo measurement of hard tissue. I came into contact with the department both through my studies at the Faculty of Dentistry, Semmelweis University Budapest, where I became interested in the subject of bone substitutes, and at a KAIROS summit where I met Miklos Weszli and Arpad Schindler who had already established connections with the department.

My goal is to get as much experience with the area where materials science meets human anatomy as possible through a PhD in the complex analysis of mandibles.

2 Bone density literature review

2.1 The rationale for looking at bone density

Most authors agree that the single most important predictor of success with dental implants is the type of bone in either the mandible or maxilla that the implant is being secured into. In this context 'bone quality' is almost identical to bone density.

The denser the bone the higher the bone surface area in contact with the implant screw [1] and thereby the lower the average stresses per unit area of the implant screw, the lower the concentration of stress in any given region of the screw surface, and the less chance of movement by the screw increasing and concentrating extra stress at any one point, leading to implant failure. The more compact, cortical bone present in a unit volume of bone, the denser it is, and while cortical bone has a fairly constant density in the region of 1.85 g/cm³, trabecular bone is less dense and varies widely, becoming obviously less dense the spongier it is and the larger the average pore size within the bone.

Several classification systems have been proposed. Misch advocates a 4-type scale from D1, primarily dense cortical bone to the softest and least dense D4, where fine trabecular bone takes up almost the whole volume. Although bone density varies predictably with position in the jaw [1] there is no strict correlation between location and density of bone. The general tendency is for anterior mandible bone to be denser than posterior mandible, anterior maxilla bone to be denser than posterior maxilla, and mandible in general to be denser than maxilla. This means that classifications of bone 'quality' or density into groups, advocated by a variety of researchers in the past, vary with jaw position loosely but not strictly. While Misch cites likelihoods of 65% of anterior maxilla bone being the moderately soft D3 and 0% of the anterior maxilla being the densest D1 type for example, there is no oral region populated by entirely one category of bone density, nor is there is a bone density category that occurs only in one oral location.

Assessment of bone density assists greatly in the planning of implant surgery therefore. The likely stability of the implant varies strongly with the density of the underlying bone, and bone density can vary from location to location inside the oral cavity over quite small distances, and if dentists knew where unusually soft, low-density regions of bone were in advance, this would enable them to avoid fastening an implant (or varying the type of implant to be secured) into precisely that region. There is often discretion to secure the same implant by fastening into another region of bone a few millimetres away from the low-density zone if there was better pre-operative data about small-scale variations in bone density.

Since it is not a trivial problem to reliably detect bone density even from oral location, there is a challenge to find non-invasive ways to detect bone density in a patient before beginning surgery.

Rapidly developing scanning techniques since the 1980s have held out the promise of mapping bone density in sufficiently fine-grained detail to significantly improve the success rates of dental implants as well as many other surgical procedures involving bone. It is useful to review here the work done on developing and testing these scanning techniques over the last two decades.

2.2 Body scanning techniques and bone density

Many researchers have hailed the arrival of new scanning techniques as crucial to more accurately understanding how particularly trabecular bone internal structure behaves under mechanical load, and which features accurately predict for bone failure.

The term 'bone density' underwent changes over the period between 1985 and 2005, partly due to two effects. These were changes in the quality and repertoire of scanning techniques, and changes in the nature of studies that pair a scan with some mechanical tests. This category of studies hope to find a close enough correlation between a mechanical property and a property visible in a scan alone that future dentists and osteopaths can use scans to estimate in advance what they will encounter in planned surgery on a given patient. If some scan-visible character can be found that proves to be an accurate predictor of a mechanical property, then scans become immediately more meaningful in pre-operative clinical practice.

Examining the wide range of trabecular bone found in the human body, notions of bone density took centre stage early on, although in pre-1995 papers these are dominated by bone-mineral density (BMD). BMD is detectable by radiographic scans, and relatively straightforward to check on samples by ash tests, using a measure like the ash fraction – the weight ratio of bone burnt to ash in an oven at 700 degrees Celcius over 24 hours to the apparent volume of the original bone [2].

Since there have long been known to be density-dependent effects and mineral-content effects, particularly with elderly patients suffering from forms of bone thinning and mineral leaching, such as osteoporosis, early researchers using body scans were naturally motivated to look for a triad of:

- i) mechanical weakness and low density of total bone in trabecular bone tissue
- ii) chemical changes such as reduced presence of certain minerals
- iii) scan-visible evidence of (i) and (ii).

This early interest in BMD was a very natural consequence of legacy X-ray techniques and also a clinical dominance within osteopathy of research interest in elderly patients suffering fractures due to loss of bone density and strength [3] – alongside another research tradition of interest in children's bone growth [4]. The dental parallel to this identification of bone weakness with demineralisation is the thinning of bone within toothless sections of the mandible, as reduced mechanical stresses on that part of the jawbone [5, 6] lead to the constant remodelling process within live bone reallocating minerals and tissue density away from that less-used jaw region to elsewhere within the skeleton.

However, BMD is mineral-centric and by itself ignores the single most interesting and important feature of trabecular, spongy, or cancellous bone, which is its porous quality. The bubbles and cavities of trabecular bone sacrifice some mechanical strength to win a major reduction in weight, and the irregular-honeycomb-style internal structure (a structure moreover which undergoes constant subtle changes of micro-shape during remodelling in live bone) is overlooked in mineral-content calculations. Strut and fibre shapes within trabecular bone matter for analysing its mechanical properties, and though most researchers carefully avoid this danger, those who focus on bone-mineral density run the risk of attending overly to chemical composition and forgetting physical structure. As a result a major set of researchers [6, 7, 8, 9, 10] addressed and continue to address this mismatch explicitly. Their studies search for the missing link between radiologically visible mineral content and performance by bone samples in arrays of mechanical tests, many of which consciously look at and try to model trabecular structure.

In addition, further refinement of scanning techniques has made straightforward radio visibility of certain minerals in bone less important as improved resolution gives clinicians a chance to see finer-grained structures in bone with acceptable doses of low radiation to patients. The addition of magnetic resonance imaging (MRI) [3] and ultrasonic imaging [11] has also made minerals less decisive. However, for many authors, the phrase 'bone density' still means BMD or bone-mineral density. To express the more straightforward idea of bone versus marrow (or whatever other materials or fluids fill the gaps inside trabecular bone) the phrase 'bone volume fraction' has become common [12].

This study will use 'bone density' as interchangeable with 'bone volume fraction' and never to indicate bone-mineral density unless explicitly stated. A shift to bone volume fraction as the single most important scan-visible property in newer scanning techniques is a natural effect of improved resolution and detail. With this is passing another category of research papers, concerned mainly with calibrating machines to each other [13] and tackling resolution problems with the machines such as visual artifacts [14]. Simply obtaining some reliable numbers indicative of bone presence is no longer the state of the art, and as fine structure emerges in greater detail a large-scale shift has taken place in research in this field.

Studies on pairing finite-element (FE) models aiming at understanding of this honeycomb-like architecture within the range of varieties of cancellous bone with bone-mineral density are giving way to pairing these or other FE models with bone volume fraction increasingly detectable and visible in newer types of scan. Behind this is a secondary shift in which the improved quality and sophistication of scanning techniques since 2005 are in turn refining the FE models. More exotic modelling techniques drawing on topology [15], fractal dimensioning [9], or fuzzy logic [16] are evidence for the way that this research area is changing.

Less and less a field which pairs low-resolution X-ray-style data with physics concepts drawn from statics and structural engineering (beams, struts, etc), it is becoming a field which pairs higher-resolution and lower-radiation data with more esoteric mathematical techniques better suited to understanding biological composite materials as something richer than merely miniature bridges built out of bone equivalents of girders and scaffolding.

In this context the general challenges are to

- i) develop better FE models modelling trabecular bone's anisotropic ability to bear directional loads (in part this rests on improved scanning and visualisation software), and
- ii) improve the understanding and measurement of volume fraction (true bone density) that gives the FE models of (i) numerical substance and accuracy in clinical use.

2.3 Pre-1990s papers

In 1987 Cullum, Ell, and Ryder reviewed dual-photon X-ray absorptiometry (DEXA) as a new and safer method for measuring bone density – as noted above, this term here means bone-mineral density as opposed to physical density of bone tissue per unit of volume.

2.4 Papers reviewing the field

Odgaard in 1997 reviewed various techniques for 3D imaging of trabecular bone and 3D quantification of trabecular architecture. This article looks at different techniques for 3D imaging, including serial sectioning, X-ray tomographic methods, and NMR scanning [18].

Tyndall et al in 2012 published a review [19] of the literature on maxillofacial cone-beam computed tomography (CBCT) so as to update the 2000 position statement on criteria for radiology in implant dentistry for the American Academy of Oral and Maxillofacial Radiology. This document summarises scanning techniques and dental applications in the field to date.

Tyndall's team has particular caveats about current methods for classifying jawbone quality. "It is generally agreed that the success of dental-implant placement depends on oral bone quality. Currently, however, there is no agreed on definition for the term "bone quality" and no agreed on method for assessing bone quality."

"Bone quality is considered good when there is enough cortical and trabecular (cancellous) bone to hold the implant securely (which is required for osseointegration) and is considered poor when there is inadequate oral bone to hold the implant securely. Based on the abundance of published articles on assessments of osteoporosis risks, there is little doubt that oral-radiographic procedures are useful in assessing bone quality; however, few studies have been devoted to assessing oral-bone quality for implant placements. The most commonly used classification system for assessing oral-bone quality for implant placement was introduced in 1985 and uses 4 radiographic oral-bone classes that are based on visual assessments of the amounts of the cortical and trabecular bone". [their reference Lekholm U, Zarb GA. Patient selection and preparation. In: Branemark PI, Zarb G, Albrektsson T, editors. Tissue integrated prostheses. Osteo-integration in clinical dentistry. 3rd ed. Chicago: Quintessence Publishing; 1985. p. 199-209.]

Tyndall et al conclude *"The use of dental-radiographic trabecular features for the assessment of implant sites has received little research attention other than visual assessments of dense and sparse trabeculation on radiographic images.*[their reference Ribeiro-Rotta RF, Lindh C, Rohlin M. Efficacy of clinical methods to assess jawbone tissue prior to and during endosseous dental implant placement: a systematic literature review. Int J Oral Maxillofac Implants 2007;22:289-300.] *Although several radiographic methods for assessing alveolar-bone quality have been suggested, no method has been tested in large clinical trials and no method can be recommended at this time. Better assessments of bone quality may influence surgical technique, implant selection (i.e., length, diameter, and type) and the loading protocol. Research in this area is needed."*

Andrew Burghardt and co-authors give a review [20] of differing scanning techniques, particularly varieties of computed tomography, for imaging bone and assessing bone quality.

2.5 Scanning techniques and their limitations

Hui, Gao, et al cross-calibrated three different dual-photon X-ray absorptiometry (DEXA) machines in 1997 to reduce inconsistencies and to devise a standard version of bone-mineral density (BMD) named standardised bone-mineral density (sBMD). This work recognised that, although DEXA had become a vital scanning tool for measuring bone characteristics non-invasively, it retains distinctive problems, particularly with calibration of different manufacturers' models [13].

A team led by Katsumata investigated a sometimes reported image artifact seen in limited-volume cone-beam computed tomography (CBCT) using a plastic water-filled cylinder as a phantom for the human head. A correlation was found between the artifact and the CT value of the object, and the authors suggested that a halo effect from the image intensifier system is responsible [14].

Katsumata, Hirukawa et al scanned a set of test objects, vertebrae and mandible parts, in order to assess the effects of maxillofacial hard tissue structures outside the reconstructed volume during cone-beam computed tomography (CBCT) imaging. Other researchers had reported that hard tissues outside the volume sometimes affect the density values obtained for hard and soft tissue structures within the volume. There were also reports that the size of this effect varies with the size of the scanned volume. They found that there was variation with the size of the scanned volume, an inverse relation as large scanned volumes were relatively free of the effect. Density also varied when objects outside the volume were increased in number.

Pinsky, Pinsky, Dyda et al carried out an in vitro validation study to establish whether linear and 3D cone-beam computed-tomography (CBCT), using volumetric measurements, is accurate for determining osseous defect sizes [21]. The authors finish by predicting “It is expected that future software development will also simplify automated determination of defect volume, regardless of their anatomic localization and shape.”

A team led by Lagravere investigated the effect of an object’s location in a cone beam CT imaging chamber on its apparent density and to develop a linear conversion coefficient for Hounsfield units (HU) to material density for the NewTom 3G Scanner [22]. They concluded that a linear relationship can be used to determine the density of materials in the density range of bone from the HU values of a CBCT scan.

McCance led a team devising a new method of colour-coding three-dimensional images to show bone position and soft-tissue-to-bone ratios after surgery, using superimposed CT scans. A Hounsfield Unit rating of 150 was used as the threshold for distinguishing bone [23].

In 2010 a team led by Hohlweg-Majert investigated whether bone quality and quantity were successfully evaluated and measured by cone-beam computed tomography (CBCT) together with image analysis. Sample cylinders and pig skull halves were used to calibrate the accuracy of the scan, comparing CT to CBCT in Hounsfield units. They concluded that cone-beam computed tomography analyses bone mass well, but not bone quality [24].

In 2002 Taylor et al reported that, despite detailed geometrical and density information from computed tomography (CT) scanning, at that date a good

method for predicting mechanical properties of bone from bone-density measurements had yet to be made available [25].

In 2010 Issever, Link et al compared magnetic resonance imaging (RTI) to quantitative computed tomography (QCT) for bone visualisation [26].

2.6 Better visualisations of scan data

A team led by van Rietbergen in 1995 devised a method for directly transforming computed-tomography scan voxels into elements for a finite-element-analysis (FEA) interpretation of loading stresses and responses on trabecular bone. Their approach resolved a 5mm cube of trabecular bone into 296,679 elements. Comparing their model with experimental data from other researchers in the literature they concluded that deformation of the trabecular bone in the cube was most marked under bending loads [27].

In 1998 Laib and Ruegsegger compared approaches for interpreting 3D models of trabecular bone extracted from computed tomography or magnetic resonance imaging scans. They found an earlier approach based on bone surface and volume ratios, modelling structure in terms of idealised plates performed less well than extracting first the skeleton from the image, calculating trabecular number, and then deriving average trabecular thickness densitometric bone volume fraction [28].

A team led by Reina in 2007 used mathematical models of bone remodelling to predict distribution of bone-density and elastic constants in a human mandible as a contribution towards creating finite-element models for simulating the mechanics of mandibles [29]. Particular attention was paid to reproducing experimentally-found levels of bone anisotropy, a feature missing from many models devised by other researchers to date working on the mandible. Anisotropic features had been captured more successfully by workers in the field modelling the mechanical behavior of the human femur, so Reina et al reused a femur-based model and applied these parameters to the mandible, reaching a reasonable level of agreement between clinical studies and their numerical predictions.

Computed tomography images were selected by Hyo-Sang Park's team from 23 men and 40 women and bone density was measured at a range of sites using V-Works imaging software [30]. Density of the cortical bone was greater in the mandible than in the maxilla and showed a progressive increase from the incisor to the retromolar area, perhaps valuable information when selecting sites and placement methods for miniscrew or microscrew implants in the dental arch.

Christian Hellmich's team proposed a way to obtain stiffness tensors of human mandible bone operating on Hounsfield units from the same X-ray data used to

calculate the Hounsfield values [31]. Based on voxel average rules for the X-ray attenuation coefficients, they assigned to each voxel the volume fraction occupied by water (marrow) and that occupied by solid bone matrix. With a continuum micromechanics representation for bone based on voxel-invariant (species and whole bone-specific) stiffness properties of solid bone matrix and of water, they converted the volume fractions into voxel-specific orthotropic stiffness tensor components. The micromechanics model, in combination with the average rule for X-ray attenuation coefficients, predicts a quasi-linear relationship between axial Young's modulus and HU, and highly nonlinear relationships for both circumferential and radial Young's moduli as well as for the shear moduli in all principal material directions.

Kaki et al assessed the three-dimensional (3D) distribution of the most mineralised cortical bone in 32 subjects with asymmetrical mandibles using quantitative computed tomography (QCT) [32]. Their study found a high degree of correlation for the shorter side of the asymmetrical mandible with higher levels of mineralisation.

Panagiotopoulou, Curtis, et al tested the strength of macaque mandibles by comparing direct mechanical measurements against mathematical predictions derived from a finite element analysis (FEA) model of the mandible constructed using computed tomography (CT) images [33]. They found that when given a suitable Young's modulus value the fine detail of subcortical mandible structure could be modelled as a solid.

2.7 Clinical studies of bone properties in situ

A team led by Elise Morgan in 2003 carried out a study [34] to characterize the contribution of inter-site differences in trabecular architecture to corresponding variations in apparent yield strains.

The group concluded that within the context of small deformations, inter-site variations in architecture do not affect apparent yield strains. However, they report that results of ancillary analyses designed to test the validity of the small deformation assumption suggested that the propensity to undergo large deformations constitutes an important contribution of architecture to inter-site variations in apparent compressive yield strains.

Michael Jaasma et al studied three trabecular bone specimens to assess the effects of intraspecimen variation for tissue modulus [35]. They concluded that intraspecimen variations in tissue modulus, if large, may have appreciable effects on trabecular apparent modulus and tissue-level failure. The observed effects depended on the assumed spatial distribution of the tissue modulus variations, a description of such distributions, particularly as a function of age, disease, and drug treatment, may provide new insight into trabecular bone structure-function relationships.

In 1998 Fazzalari and colleagues tested samples of trabecular bone obtained from 34 patients with a mean age of 70.3 years undergoing bone surgery, assessing the predictive value of bone-mineral density, not volume fraction density [36].

The authors state that data from this study suggest that bone-mineral density (BMD) and micro-crack density (Cr.Dn) are the major determinants of cancellous bone strength, whereas BMD and trabecular anisotropy are major determinants of cancellous bone stiffness.

However they warn *“In bone specimens subjected to compressive testing there was no relationship between microdamage and BMD, suggesting that BMD cannot be used to monitor changes in the mechanical properties of bone due to microdamage accumulation.”*

Tang and Vashishth performed a study in 2007 which found that damaged volume fraction (DV/BV), as determined by microCT, increased exponentially with respect to applied strains and proportionately to mechanically determined modulus reduction ($p < 0.001$) [37].

They remark *“Furthermore, the formation of microdamage was observed to occur before any apparent stiffness loss, suggesting that the localized tissue yielding occurs prior to the structural yielding of trabecular bone.”*

Turkyilmaz et al carried out computerized tomography (CT) for pre-operative evaluation of the jaw bone for each of 108 patients receiving dental implants in an investigation to check correlation between bone density, insertion torque, and implant stability [38]. Statistically significant correlations were found.

2.8 Attempts to reconcile scan data with mechanical tests

Peter Augat et al reported in 1997 experiments on 97 cubic samples of trabecular bone to scan them using computed tomography (CT) and then tested multi-directionally to assess their directional anisotropy and compare this to bone mineral density (BMD) [39].

They found that BMD had the greatest predictive value for deriving mechanical properties in the principal loading direction.

Hernandez et al in 2001 [40] derived an expression for bone volume fraction as a function of apparent density and ash fraction to re-analyse data presented by Keller in 1994.

“Mechanical testing of bone samples has identified the apparent density (mineralized bone mass/bulk volume) and the ash apparent density (ash mass/bulk volume) as effective predictors of bone strength and stiffness.” * Martin, R. B., Burr, D. B., and Sharkey, N. A. Skeletal Tissue Mechanics. New York: Springer; 1998.

“One limitation of models based on apparent density or ash apparent density is that they do not separate the influence of bone volume fraction from that of ash fraction.”

On the topic of apparent bone ash density, Hang Yao in ‘Mechanical Testing of Bone and Bone-Like Materials...’, page 11, that

“The apparent density of hydrated human cortical bone is about 1.85g/cm cubed, and varies little from site to site. In contrast the average apparent density of trabecular bone depends greatly on anatomic site. It is as low as 0.10g/cm³ for the elderly spine, about 0.30g/cm³ for the human tibia, and up to about 0.50g/cm³ for the load-bearing portions of the proximal femur. After skeletal maturity (around age 25), trabecular bone apparent density decreases with ageing..... Ash densities, tissue and apparent, can be obtained when the bone is deorganified by heating it in a furnace for 24 hours at 700 degrees C, thereby removing all water and organic material. The ratio of ash weight to dry weight is often used to describe the percentage mineralisation, or ash content, of bone tissue, regardless of whether it is cortical or trabecular bone.The wide variation in density for trabecular bone results in a much greater heterogeneity in its material properties compared with cortical bone. Given this heterogeneity, it is rarely adequate to discuss the biomechanical properties of trabecular bone without reference to its apparent density (or volume fraction).”

Sanyal et al mechanically analysed 54 specimens in the form of 5mm cubes of human trabecular bone taken from 44 different cadavers [41]. The specimens came from four anatomic sites, and bone volume varied widely from 0.06 to 0.38.

The team found that the computed values of both the shear and compressive strengths depended on bone volume fraction via power law relations having an exponent of 1.7. The ratio of shear to compressive strengths did not depend on bone volume fraction but did depend on microarchitecture, most notably the intra-trabecular standard deviation in trabecular spacing. For shear, the main tissue-level failure mode was tensile yield of the obliquely oriented trabeculae. By contrast, for compression, specimens having low bone volume fraction failed primarily by large-deformation-related tensile yield of horizontal trabeculae and those having high bone volume failed primarily by compressive yield of vertical trabeculae. Their conclusion was that human trabecular bone is generally much weaker in shear than compression at the apparent level, reflecting different failure mechanisms at the tissue level.

Bevill et al are critical of bone-strength models relying overly on bone-density measures [42]. Their study warns that over-reliance on bone volume fraction in assessing trabecular strength risks under-estimating the role in predicting bone failure of anisotropic strength along particular axes of rigidity – and its absence in other axes – within cancellous bone.

Bevill, Farhamand, and Keaveny sought to address anisotropy of trabecular yield strains while accounting for variations in both density and anatomic site and to

determine the underlying mechanisms. They cored cylindrical specimens from vertebral bodies and femoral necks with the principal trabecular orientation either aligned along the cylinder axis or at an oblique angle of 15° or 45°. Each specimen was scanned with micro-CT, mechanically compressed to failure, and analysed with nonlinear micro-CT-based finite element analysis.

Yield strains depended on anatomic site, and the effect of off-axis loading was different for the two sites—yield strains increased for off-axis loading of the vertebral bone, but were isotropic for the femoral bone. With sites pooled together, yield strains were positively correlated with bone-volume/tissue-volume (BV/TV) for on-axis loading, but no such correlation existed for off-axis loading. Analysis of the modulus-BV/TV and strength-BV/TV relationships indicated that, for the femoral bone, the reduction in strength associated with off-axis loading was greater than that for modulus, while the opposite trend occurred for the vertebral bone. The micro-FE analyses indicated that these trends were due to different failure mechanisms for the two types of bone and the different loading modes. They report their results provide insight into the failure behavior of human trabecular bone and highlight the need for a multi-axial failure criterion that accounts for anatomic site and bone volume fraction.

Morgan et al also express scepticism that there is a strong relationship between elastic-modulus and density in trabecular bone that overrides the importance of anatomic site [43]. Unlike Bevilacqua and colleagues, Morgan's team investigated *on-axis* loading strains in cancellous bone, and again found factors other than density predicting failure better than density.

They obtained 142 specimens from 61 cadavers (mean age 67 years) and used a high-resolution finite-element (FE) model to test for on-axis elastic moduli. This was compared to apparent density. Resultant power law regressions between modulus and density did depend on anatomic site, as determined via an analysis of covariance. The inter-site differences were among the leading coefficients ($p > 0.02$), but not the exponents ($p > 0.08$), which ranged 1.49–2.18.

At a given density, specimens from the tibia had higher moduli than those from the vertebra and femoral neck; those from the trochanter had higher moduli than the vertebra. These differences could be as large as almost 50%, and errors in predicted values of modulus increased by up to 65% when site-dependence was ignored. Tissue moduli computed using methods that account for inter-site architectural variations did not differ across site ($p > 0.15$), suggesting that the site-specificity in apparent modulus–density relationships may be attributed to differences in architecture.

“These results indicate that there is no universal modulus–density relationship for on-axis loading.” Morgan et al say, summing up.

In a separate study [44] Morgan and Keaveny investigated uniaxial tensile and compressive yield properties of trabecular bone for cylindrical specimens from the vertebra, proximal tibia, femoral greater trochanter, and femoral neck taken from the same 61 donors, mean age 67, also reported on by Morgan, Bayraktar, and Keaveny.

Again they emphasise anatomic site over bone density. The compressive yield strain was higher for the femoral neck than for all other sites, as was the tensile yield strain for the vertebra. They emphasise that analysis of covariance, with apparent density as the covariate, indicated that inter-site differences existed in yield stress even after adjusting statistically for density.

A team led by Noel Harrison tested cuboid trabecular bone samples taken from eight, 4-year- old (skeletally mature) ovine L5 vertebrae as part of a new approach to determine heterogeneous bone tissue material properties for computational models [45]. These models, equipped with parameters obtained from nano-indentation tests, use high-resolution voxel-based finite element software to study trabecular bone at the micro-scale.

They determined the specimen-specific range of tissue moduli across strut width from nano-indentation testing. This range was mapped directly using linear interpolation to that specimen's micro-computed tomography (μ CT) grey value range as input material properties for finite element analysis. Before undergoing experimental uniaxial compression tests, the samples were μ CT-scanned and 30 μ m-resolution finite element models were generated. The linear elastic finite element models were compressed to 1% strain. This material property assignment method for computational models accurately reproduced the experimentally determined apparent modulus and concentrations of stress at locations of failure.

In 1998 Uchiyama and colleagues investigated how well bone-mineral density (BMD) (not volume fraction) correlated with other measures of mechanically tested trabecular bone strength [9]. Their preliminary study showed that: (1) bone mass index is correlated with mechanical properties, with coefficients of correlation ranging from 0.552 to 0.601; and (2) when controlling for BMD, no association could be detected between measures of structural complexity (connectivity density and fractal dimension) and elastic modulus in the craniocaudal direction of human vertebral bodies.

The authors suggest they might be the first to mention fractal dimension as a possible way to classify types of trabecular bone in terms of internal structure. *“Odgaard provided a detailed review of three-dimensional methods for quantifying trabecular bone microstructure, but did not mention fractal dimension. We presume that the current study is the first to calculate the fractal dimension of trabecular bone in three dimensions using micro-CT. “*

In 1998 Kopperdahl and Keaveny reported a study [46] to test whether on-axis yield strains are independent of trabecular bone density with reference to adaptive remodelling in the bone to maintain a constant safety factor.

To test the hypothesis that yield strains are indeed independent of density, compressive and tensile yield strains were measured without end-artifacts for low density human vertebral trabecular bone specimens. Loads were applied in the

superior—inferior direction along the principal trabecular orientation. These ‘on-axis’ yield strains were compared to those measured previously for high-density bovine tibial trabecular bone. Mean yield strains for the human bone were $0.78 \pm 0.04\%$ in tension and $0.84 \pm 0.06\%$ in compression; corresponding values for the bovine bone were 0.78 ± 0.04 and $1.09 \pm 0.12\%$, respectively. Tensile yield strains were independent of the apparent density across the entire density range. By contrast, compressive yield strains were linearly correlated with apparent density for the human bone and the pooled data, and a suggestive trend existed for the bovine data.

These two researchers claim that their results refute the hypothesis that on-axis yield strains for trabecular bone are independent of density for compressive loading, although values may appear constant over a narrow density range.

In 2004 Harun Bayraktar and Tony Keaveny tested high-resolution finite-element models of 12 human femoral neck trabecular bone specimens in order to investigate why variations in yield strains for trabecular bone within a specific anatomic site are only a small fraction of the substantial variations that exist for elastic modulus and strength [47]. Again, bone density was discounted as a major source of intersample variation.

The finite element models, used to obtain apparent yield strains in both tension and compression, assumed that the tissue-level yield strains were the same across all specimens.

Comparison of the model predictions with the experimental data therefore enabled them to isolate the combined roles of volume fraction and architecture from the role of tissue material properties. Results indicated that, for both tensile and compressive loading, natural variations in volume fraction and architecture produced a negligible coefficient of variation (less than 3%) in apparent yield strains. Analysis of tissue-level strains showed that while bending of individual trabeculae played only a minor role in the apparent elastic behavior, the combined effects of this bending and tissue-level strength asymmetry produced apparent-level failure strains in compression that were 14% lower than those at the tissue level. By contrast, Bayraktar and Keaveny reported that tissue and apparent-level yield strains were equivalent for tensile loading.

They concluded that the uniformity of apparent yield strains is primarily the result of the highly oriented architecture that minimizes bending. Most of the variation that does occur is the result of the non-uniformity of the tissue-level yield strains. They conclude by warning that *“Despite the strengths of this study, certain caveats exist. For low volume fraction trabecular bone, in which nonlinear deformations such as bending and buckling may play a more important role (Bayraktar et al., 2003; Kopperdahl and Keaveny, 1998; Müller et al., 1998; Snyder et al., 1991), our conclusions must be extrapolated with caution. While these deformations will cause a greater difference between the tissue and apparent-level yield strains for compression—a result of the increase in*

compliance due to geometrically nonlinear deformations in bending—in tension, the slightly oblique trabeculae will further align with the loading direction so that tissue yield strains in tension would be expected to remain equivalent to those at the apparent level.”

A team led by P.J. Thurner presented results in 2006 of experiments in high-speed photography of bone (both cortical and trabecular) samples during mechanical compression tests, with a view to seeing fracture bands forming in trabecular bone during failure [48].

The authors state that to overcome the limitations of standard mechanical tests delivering merely integral information about complicated samples, experiments were designed for step-wise mechanical testing with concurrent imaging of trabecular and cortical bone. They carried out real-time imaging of trabecular bone during compression using high-speed photography and investigated whether the whitening of deformed trabeculae is due to micro-damage.

Strongly deformed trabeculae were seen to whiten, an effect similar to stress whitening in polymers. Scanning Electron Microscopy of the same regions of interest revealed that whitened trabeculae were strongly damaged by microscopic cracks and mostly failed in delamination.

A team led by Lettry in 2003 [49] investigated Young’s modulus values in five freshly donated human mandibles, aiming to correlate computed tomography (CT) scan numbers with directional mechanical properties of the bone so as to help develop more accurate non-invasive ways to assess bone hardness and rigidity before implant surgery. Their mechanical testing produced lower e-modulus values than a previous study on dry mandibles, and they found only a low correlation between the CT numbers and the modulus, concluding more work was needed in order to better evaluate bone characteristics from CT scan data only.

Stoppie, Pattijn et al [10] obtained Hounsfield values from a computed tomography (CT) scan of bone samples from eight jawbones and compared these to Young’s modulus calculations derived from compression tests on the same samples, bone mineral density (BMD) using a dual energy X-ray absorptiometry scan, and bone volume calculations among other tests. Their conclusion that predictions of mechanical properties of trabecular bone based on Hounsfield values decline in accuracy in mandibles with thicker coatings of cortical bone show the limitations of relying on a single measure to estimate a complex concept such as material strength. They write “*Fanuscu & Chang (2004) described the microstructure of trabecular bone in the mandible and maxilla of one cadaver. They found a wide variation of bone density irrespective of the amount of cancellous bone. In contrast to a precise determination of bone volume (BV), bone quality is usually assessed by a crude grading method.*”

Stoppie, Pattijn and colleagues continue describing problems with classifying bone quality, particularly for cancellous bone. *“For pre-operative clinical assessment, Lekholm & Zarb (1985) suggested a bone classification based on macrostructure where the morphology and distribution of cortical and trabecular bone determined the quality. Lindh et al. (1996) found that it was impossible to evaluate the accuracy of the proposed classification because of a wide variation of inter-observer (between 49% and 64%) as well as of intra-observer agreement (between 75% and 86%). They proposed a new classification with reference images to assess the trabecular pattern in periapical radiographs before implant treatment. Norton & Gamble (2001) concluded that there is a need for an objective quantitative classification of bone quality, which can be applied pre-operatively and is not operator dependent. They proposed a new classification based on the Hounsfield units of the bone on the CT scan and related it to the existing classification of Lekholm & Zarb (1985).”*

Stoppie et al sum up the state of affairs as it was in 2005. *“A new pre-operative classification of bone quality is mandatory. As CT is becoming a standard procedure in the preoperative planning of dental implants, the Hounsfield units of the selected implant sites are available and a classification like the one proposed by Norton and Gamble in 2001 seems most suitable. The question remains as to how these Hounsfield values relate to the structural and mechanical properties of the jawbone. The aim of this study was to determine the Hounsfield values of selected jawbone sites and to investigate the relationship of these Hounsfield values with the bone mineral density (BMD) determined by the dual-energy X-ray absorptiometry (DXA) scan, the BV [bone volume] based on the micro-focus CT scan, the transmission time of the ultrasound measurement and the Young’s modulus measured with a compression test.”*

Lagravere, Fang et al compared Hounsfield units to density data obtained from cone-beam CT scans [22], and Lagravere’s team was working with more consistent samples than Stoppie’s team. Lagravere et al conducted tests on cylinders of known densities.

Once different measurement techniques were compared on a real-world composite material like the human jaw as in the work by Stoppie and Pattijn’s group, even internal structure formed from just two phases – cortical and trabecular bone – was enough to sharply reduce the predictive power of metrics that perform well on a homogeneous material such as wholly trabecular or wholly cortical bone. Stoppie et al note that Hounsfield-based predictions of mechanical strength for mandible where trabecular bone has only a thin cortical covering were substantially better than for thick-cortical mandibles. This was because those samples with a thin covering of compact tissue could be approximated as homogeneous cancellous bone, an unrealistic assumption to make with mandibles in general however.

Stoppie, Pattijn, and colleagues describe the procedure they used to mill the ends of their cylindrical samples down to exactly 8mm in length, and then say *“Despite the planning of the bone specimens on the first CT scan, the micro-CT*

images showed that for a total of 24 specimens, 13 specimens were a mix of trabecular and cortical bone, while 11 specimens were composed of trabecular bone only."

They continue "Despite the planning only 11 bone specimens were composed of trabecular bone only. A height of 8mm was required for the compression test and in order to reach this length, a number of bone specimens had to be planned reaching the cortical–trabecular border."

"After trepanation, the micro-CT images revealed that a thin border of cortical bone was still present at the top and bottom of the specimen. The mixed specimens in this study were composed of approximately 90% of trabecular bone and only 10% of cortical bone. For specimens of only cortical bone, the literature shows no or low correlations between Hounsfield values and mechanical properties (Snyder & Schneider 1991; Rho et al. 1995). For this reason, the 11 trabecular bone specimens were considered separately during data analysis."

Bilhan, Arat, and Geckili [50] tested extracted cylinders of cadaver mandible bone by comparing CT-scan information and macroscopic examination for assessment of bone density, and concluded that Hounsfield units alone provide a misleading measure of bone density. As with the Stoppie team study, Bilhan et al found undesirably large variations between the two approaches to density estimation, again casting doubt on the reliability of CT-derived data effectively interpreting mandible or other bone as a routinely homogeneous rather than heterogeneous material.

Bilhan's team emphasise the central role of bone density in evaluating dental-implant-site suitability. *"Bone density plays an important role in planning of implant dentistry in terms of timing of loading as well as number of implants to be used for denture support especially in critical locations such as posterior maxillae. Bone mass, structural properties (macro- and microarchitecture), and material properties (modulus of elasticity, mineral density, etc.) constitute mechanical competence of bone, which is commonly referred to as bone quality in implant dentistry [they refer to M. I. Fanuscu and T. L. Chang, 'Three-dimensional morpho- metric analysis of human cadaver bone: microstructural data from maxilla and mandible,' Clinical Oral Implants Research, vol. 15, pp. 213–218, 2004.]"*

Bilhan, Arat, and Geckili continue on the shortcomings of some current approaches to bone density. *"Substantial variations in bone quality in corresponding anatomical sites and direct correlation between bone quality and implant success rates exist [their reference here is T. Jemt and U. Lekholm, 'Oral implant treatment in posterior partially edentulous jaws: a 5-year follow-up report,' International Journal of Oral and Maxillofacial Implants, vol. 8, no. 6, pp. 635–640, 1993.].... These assessment methods have various limitations in addressing cortical and cancellous bones in an objective and quantitative manner."*

Paying particular attention to computed-tomography (CT) data expressed in Hounsfield units (HU), Bilhan et al warn “*Low dose CBCT is often advised for implant planning, considering the possibility to gather clinically relevant 3D data at a low dose, but CBCT does not necessarily allow reliable and accurate bone quality assessment when focusing on the inherent radiographic density information that is otherwise expressed by HU* [their reference A. Yamashina, K. Tanimoto, P. Sutthiprapaporn, and Y. Hayakawa, ‘The reliability of computed tomography (CT) values and dimensional measurements of the oropharyngeal region using cone beam CT: comparison with multi-detector CT,’ *Dentomaxillofacial Radiology*, vol. 37, no. 5, pp. 245–251, 2008.]”

They continue, quantifying the shortcomings of over-relying on Hounsfield numbers. “*Although strong correlations exist, still a 30–50% of unaccounted variance in mechanical properties from bone density measurement has been reported* [their references T. M. Keaveny and O. C. Yeh, ‘Architecture and trabecular bone—toward an improved understanding of the biomechanical effects of age, sex and osteoporosis,’ *Journal of Musculoskeletal Neuronal Interactions*, vol. 2, no. 3, pp. 205–208, 2002 and G. H. van Lenthe, J. P. W. van den Bergh, A. R. M. M. Hermus, and R. Huiskes, ‘The prospects of estimating trabecular bone tissue properties from the combination of ultrasound, dual-energy X-ray absorptiometry, micro-computed tomography, and microfinite element analysis,’ *Journal of Bone and Mineral Research*, vol. 16, no. 3, pp. 550–555, 2001.]”

“*Osteoporotic cancellous bone is characterized by low bone mass as well as a deterioration of the microarchitecture. Whether a patient is diagnosed osteoporotic depends only on his/her BMD and how this BMD value compares to a population average* [Bilhar and team refer to J. A. Kanis, ‘Osteoporosis III: diagnosis of osteoporosis and assessment of fracture risk,’ *The Lancet*, vol. 359, no. 9321, pp. 1929–1936, 2002.]”

“*Clinical results have shown that BMD of patients with osteoporotic bone fractures and patients without such fractures can have a substantial overlap* [their reference S. Majumdar, H. K. Genant, S. Grampp et al., ‘Correlation of trabecular bone structure with age, bone mineral density, and osteoporotic status: in vivo studies in the distal radius using high resolution magnetic resonance imaging,’ *Journal of Bone and Mineral Research*, vol. 12, no. 1, pp. 111–118, 1997.], *causing variance similar to that in density—mechanical property relationship studies. The microarchitecture of cancellous bone has been largely attributed to this variance; density approximates the amount of bone tissue within a cancellous bone specimen but it does not quantify the microarchitecture that is inherent. Together with bone density readings, a quantitative measurement of microarchitectural parameters may improve our ability to better estimate bone strength* [their reference H. K. Genant, C. Gordon, Y. Jiang, T. F. Lang, T. M. Link, and S. Majumdar, ‘Advanced imaging of bone macro and micro structure,’ *Bone*, vol. 25, no. 1, pp. 149–152, 1999.]”

The authors spell out their main result in comparing CT and micro-CT scans of mandible bone. *“The bone cylinder which was scanned by micro-CT showed an incongruous structure when HU of the donor site was considered. The HU values indicated a higher density bone, whereas the Micro CT image revealed rather a spongy bone”*

2.9 Work to improve finite-element models of bone properties

A team led by G.H. van Lenthe reported a study aiming to improve the accuracy of mechanical-behavior simulation of trabecular bone in finite-element (FE) models by attempting to replicate the results of micro-finite-element (μ FE) modelling at larger scales, thereby with lower computer processing costs [15]. They compared model simulation using these FE models based on CT scan results against direct strength testing of samples.

They scanned 42 human vertebral bone samples (10 mm height, 8 mm diameter) with micro-computed tomography using a 20 μ m resolution. After scanning, they carried out direct mechanical testing. They used topological classification and dilation-based algorithms to identify individual rods and plates. Two finite-element (FE) models were created for each specimen. In the first one, each rod-like trabecula was modelled with one thickness-matched beam; each plate-like trabecula was modelled with several beams. From a simulated compression test, assuming one isotropic tissue modulus for all elements, van Lenthe, Stauber, and Mueller calculated the apparent stiffness. After reducing the voxel size to 40 μ m, a second FE model was created using a standard voxel conversion technique. Again, they assumed one tissue modulus for all elements in all models, and a compression test was simulated.

Bone volume fraction ranged from 3.7% to 19.5%; Young's moduli from 43 MPa to 649 MPa. Both models predicted measured apparent moduli equally well, and were in good agreement with each other. Tissue modulus was estimated at 9.0 GPa and 10.7 GPa for the beam FE and voxel FE models, respectively. On average, the beam models were solved in 219 s, reducing central processor unit (CPU) usage up to 1150-fold as compared to 40 μ m voxel FE models. Relative to 20 μ m voxel models 10,000-fold reductions can be expected. They present a beam FE model is an abstraction of the intricate real trabecular structure using simple cylindrical beam elements. It enabled an accurate prediction of global mechanical properties of microstructural bone. They report that a strong reduction in CPU time enables increased throughput, analysis of multiple loading configuration and increased sample size, without increasing computational costs.

Niebur et al also performed a study [51] aiming to better model trabecular bone loading and failure, largely independent of bone density.

They hypothesized that high-resolution finite element models of trabecular bone

that include cortical-like strength asymmetry at the tissue level could predict apparent level failure of trabecular bone for multiple loading modes.

They applied a bilinear constitutive model with asymmetric tissue yield strains in tension and compression to simulate failure in high-resolution finite element models of seven bovine tibial specimens. Tissue modulus was reduced by 95% when tissue principal strains exceeded the tissue yield strains. Linear models were first calibrated for effective tissue modulus against specimen-specific experimental measures of apparent modulus, producing effective tissue moduli of 18.7 ± 3.4 Gpa. Next, they performed a parameter study on a single specimen to estimate the tissue level tensile and compressive yield strains. These values, 0.60% strain in tension and 1.01% strain in compression, were then used in non-linear analyses of all seven specimens to predict failure for apparent tensile, compressive, and shear loading. When compared to apparent yield properties previously measured for the same type of bone, the model predictions of both the stresses and strains at failure were not statistically different for any loading case ($p > 0.15$).

Use of symmetric tissue strengths could not match the experimental data. They report that once effective tissue modulus is calibrated and uniform but *asymmetric* tissue failure strains are used, the resulting models can capture the apparent strength behaviour to an outstanding level of accuracy.

They conclude “*these computational models have reached a level of fidelity that qualifies them as surrogates for destructive mechanical testing of real specimens.*”

Odin et al investigated the Young's modulus for mandible bone, with particular attention to the precise geometry of each bone sample [52]. They were prompted by a wide array of modulus values already in the research literature, in the hope of getting a more exact measure of the mechanical properties of the jaw bone. Their value of 3,000 Mpa is lower than typical values found by other researchers, due to, Odin et al report, their choosing larger and more clinically realistic (ie. larger) specimen sizes in an effort to take the heterogeneous character of bone better into account. They used an iterative approach based on feeding back comparison of each value to predictions from a numerical simulation in order to adjust the simulation parameters until the gap between values in the simulation and values in the mechanical tests became acceptably small.

Lakatos and Bojtar in 2012 reported a finite-element model of anisotropic trabecular-bone load-adaptation behaviour based on tensors [53]. Their approach is generated stochastically, “avoiding the need for CT imaging” using an idealisation that distinguishes ‘active’ beams from ‘passive’ beams within the cancellous bone. They use tensors to allow beams to change between active and passive to reflect adaptation patterns under different loads.

Misch, Qu, and Bidez cut 9 mandibles donated from humans aged between 56 and 90 into anterior, middle, and distal sections [54]. Then they extracted 76 cylindrical samples of trabecular bone with marrow, and compressed them vertically. They concluded that trabecular mandible bone from the anterior region has more compressive strength, higher elasticity, and greater bone density than equivalent samples from other regions. They noted that trabecular bone without the cortical plates lost elasticity, and that this was important in planning surgery for predicting implant outcomes.

Schwartz-Dabney and Dechow removed 44 cortical samples from each of 10 adult fresh edentulous mandibles and tested them for cortical thickness, elastic and shear moduli, orientation of axis of maximum stiffness, comparing them with results in the literature from similar but dentate mandibles [6]. They concluded that following loss of teeth, microstructural changes occur in the cortical bone of the mandible.

Fyrhie and Kimura report a mathematical development of an earlier discussion closely relating mechanical properties of cancellous bone to its biological role in metabolite diffusion [55]. Fyrhie et al in 1995 refined the relationship between bone-surface density (BS/TV) and bone volume over bone tissue fraction (BV/TV) developed originally by Martin (1984).

Nazarian et al studied 25 specimens of trabecular bone with special regard to fracture risk and bone volume fraction [56]. They report that a model with sub-regional bone-volume fraction (BV/TV) as the independent variable describes 38% of the variation in yield strength but this rises to 56% when BV/TV of the weakest sub-region is considered. Of their 25 samples 76% had minimum BV/TV in the visually determined failure regions. From these results they concluded that sub-regions with minimal bone volume to tissue volume (BV/TV, also sometimes bone volume divided by 'total' volume) are better predictors of trabecular failure than average specimen BV/TV. This percentage is given as an output by many CT scanners, but depends critically on the scanning volume chosen, giving a risk of interpretation error.

Although the areas of scanning technique, finite-element modelling, and application of results directly to clinical reality are sometimes treated separately by research teams, they equally often overlap. What remains tantalisingly out of reach is a three-way reconciliation between ever-improving 3D visualisation of real scan data; ever-faster 3D mathematical simulation of virtual loading, bone remodelling, and bone failure; and a convincing understanding of trabecular bone properties at the micro-level.

Volume-fraction bone density, and surface area per unit volume of trabecular bone, remain the missing keys to seamless interpretation and measurement.

2.10 Literature review conclusion

Numerous research teams have investigated the material and mechanical properties of bone. Knowledge of this is valuable for dental and osteopathic surgery.

The basic material properties of bone can be expressed in three relations: density, e-modulus or Young's modulus, and Poisson's ratio. Many studies attempt to obtain data for these properties, often by mechanical testing of bone extracts, sometimes donated during operations on living patients, sometimes freshly harvested from cadavers, sometimes extracted from older, dry human bone samples, and sometimes in testing on animal bone samples. Better data allows better modelling.

To date the best proxy for the sometimes ambiguous term "bone quality" is bone density. This term itself can be contentious, since some authors use "bone density" to refer to what is now more commonly called "bone mineral density". The term "bone volume fraction" best captures the more fundamental density concept ($\text{bone volume} / \text{total volume} = \text{BV/TV}$) which to date is the most straightforward bone-characteristic number and the easiest to extract from scan data.

A big advantage to bone density as a preoperative bone-quality assessment metric is that it can be measured simply and reliably in vivo. Many researchers have proposed Hounsfield units as the gold standard of bone-density measurement. However other authors like Stoppie et al point out that unexpectedly thick regions of cortical bone between the scan beam and internal trabecular regions can give the sample a Hounsfield number that poorly predicts the material properties of the heterogeneous composite sample. Authors they quote, such as Snyder and Schneider, also report poor correlation between Hounsfield units and material properties for samples of homogeneous cortical bone. Studies like these suggest it is not merely a problem with composite material internal structure – even homogeneous substances like cortical bone can show unhelpful deviation between CT-scan-generated Hounsfield numbers and material properties. Therefore scepticism is warranted regarding claims that Hounsfield numbers can alone supply definitive in vivo bone-density (volume-fraction) measurements for pre-operative treatment planning.

Researchers attempt to combine density with Young's modulus, Poisson's ratio, and other mechanical parameters so as to create and fine-tune mathematical simulations of bone behaviour in the form of finite-element (FE) models. FE models matter at this stage because, however sophisticated, they still depend on density, and caveats like those from Stoppie and Pattijn's team show that Hounsfield numbers are not always reliable predictors of bone density. Absent solid values for bone density, there are limits to what better FE modelling can achieve.

An improved way to extract reliable bone density values from scan data therefore assists the work of both finite-element modellers and clinical practioners, remembering Misch's statement that "bone density is a key determinant for treatment planning".

3 Research aims

1. To write a software program that measures area based on greyness values for CT-scanned slices of bone.
2. To use that program to add slice areas and find a value for bone-fraction volume, counting volume inside bone boundary and subtracting spaces within trabecular bone tissue from that total.
3. To test and establish this method as a better way to measure bone volume than by Hounsfield radio-density units.

4 Experiment

The specimen used was a freshly frozen mandible which the Department of Anatomy, Histology, and Embryology of Semmelweis University Budapest had harvested from a human cadaver. When handling the specimen gloves were always used. Excess soft tissue was removed and the mandible was wrapped in plastic packaging.

In order to make use of a high-resolution CT scanner (YXILON Y.CT Modular), the specimen had to be transported to the Szechenyi Istvan University of Gyor. The mandible was always kept at a constant low temperature both in Budapest and during transport to Gyor. In Gyor the specimen was placed between the X-ray source and the phosphorous screen. CT scans are ideal in this situation because the image is restricted to one slice of the specimen at a time.. Nothing below or above each individual slice affects the image. The software that was used to build images out of the scan data was VG studio 2.1, which is developed by Volume Graphics <http://www.volumegraphics.com/>

The entire specimen was scanned in one pass. Unfortunately the detector was not large enough to include the entire mandible. Therefore only the base and alveolar ridge of the mandible was scanned. The ramus and condyle were not included in the scan.

Cross section images were exported in three orthogonal directions, x, y, and z in 0.10 mm slices.

The file format of the 2-dimensional images was bitmap (BMP)

Our program was developed using MGM Design's Imaging toolkit for Delphi, which is a collection of VCL components for image scanning and processing. Direct access to individual pixels or lines in the image allows for fast manipulations of the image data in this toolkit. Some of the main program features we used were Basic Image Handling/Viewing, Math & Logic.

(<http://www.mcm-design.com/index.php?section=products&product=ImagingDelphi>)

The program we developed was tailor-made to analyse CT-scanned images of bone, and the particular challenge for the software is to locate the edges of bone regions, and to correctly identify trabeculae and soft tissues as specific regions contained within the bony structure.

First the program finds the outer contours of the mandible using previously set greyness levels. This happens in such a way that (on an already indicated setting) the program looks for the whiter colour of the bone starting from the edges of the picture and ignoring every object which is darker than the previously decided darkest bone colour. After deciding the initial contours, the software

begins scanning for trabeculae and other bone parts within the contours. Areas among the trabeculae appear in tone darker than bone, because these are the soft tissues, which are less visible in an X-ray image.

In those cases when the outer contours of the mandible are not only the colours that were set to identify bone, then the program must check whether pixels given within the contours of the mandible are or are not part of the mandible. To ensure this, the program constructs as a check process 16 lines out from every pixel. The lines are chosen at equal intervals around the 360 degrees within the CT scan picture plane. The software tests how many of these lines hit bone (or pale regions interpreted as bone). Insofar as most of the lines (this is an adjustable parameter) reach bone, then the program regards the pixel being tested as within bone, and in cases where they do not as not part of the mandible.

An initial problem with this check process was that parts outside the mandible sometimes appeared as parts within the mandible, leading us to adjust the software. We introduced a range which restricted how far lines constructed from the pixel extended. Also previously a line constructed from a point between the two segments of the arch when seen in cross-section could mistakenly give the tested pixel as being within the bone. Limiting the lengths of the lines (line length can be set in the software) avoided this error.

In cases where the outer bone coating of the mandible is not continuous and difficult for the software to decide how to connect the two sections of bone, a property of the program becomes very useful. This feature compares a layer to twenty previously analysed layers, ten above and ten below. Where a previous layer's contour is still continuous in that region, then the program on that basis brings the missing sections together in the next layer.

The range introduced above is an adjustable parameter which allows the user to set the distance between individual objects which appear as bone islands on CT cross-sections. If the two bone islands are closer to each other than a set value, then the program views them as belonging together as one single bone island.

The main goal of the program is to determine both the bone volume of the mandible and the total volume of the mandible. In the CT scan slices it measures the area of that which is enclosed by a boundary and defined as bone, taking into account the thickness of the CT scan slice, and adding to this the volume of the next bone layer. This way the bone volumes of all the layers add together to give the complete volume of the bone mass of the mandible. From the outer contours giving the total enclosed volume, the program subtracts pixels for gaps within the jawbone to give bone-mass volume.

Data in table form is exported into Excel, enabling the user to manipulate. Individual cross section images with pixel data may also be exported.

5 Data-handling and results

The specimen used in this experiment is shown in Fig. 1. Our results are based on the CT scan of this mandible.

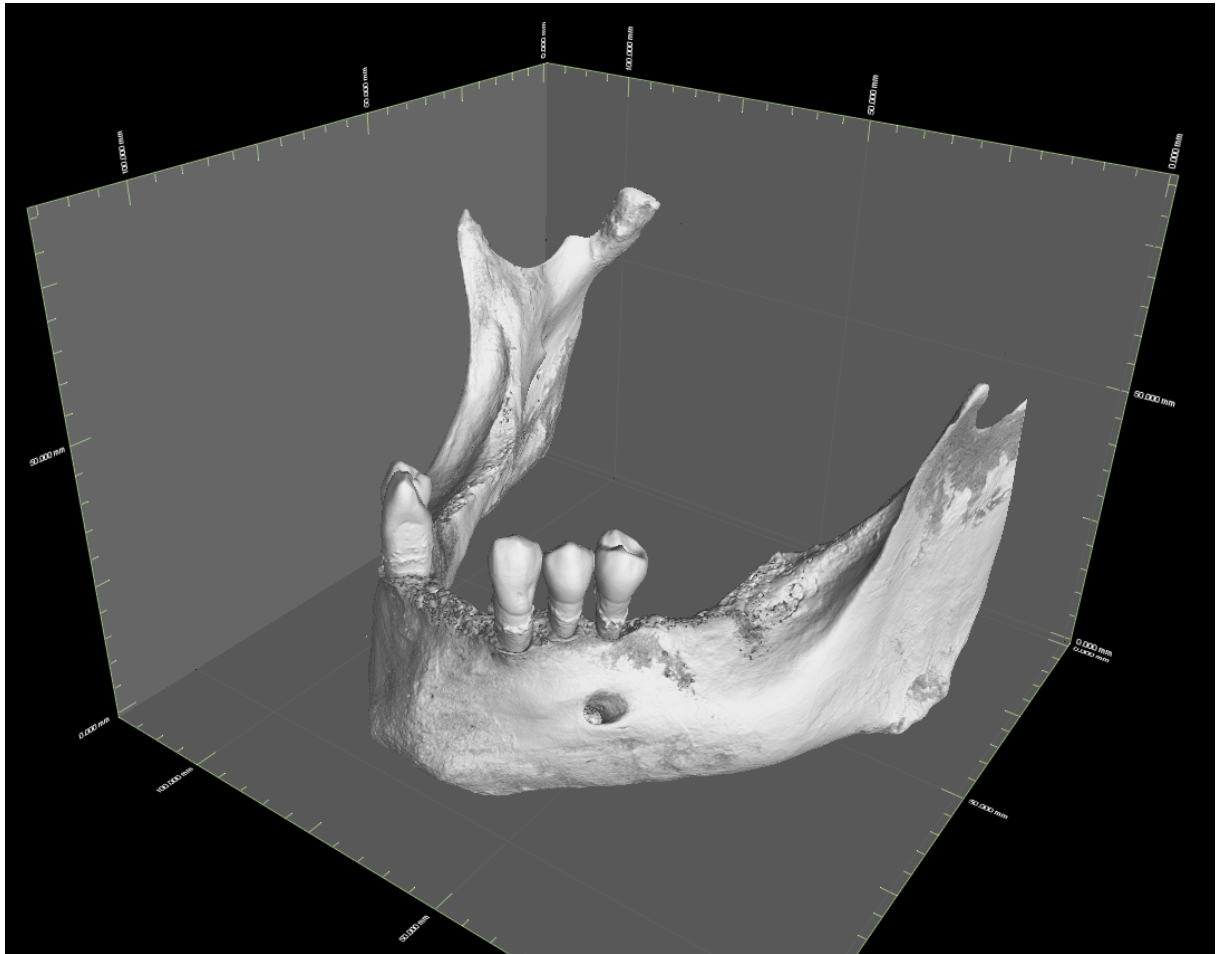
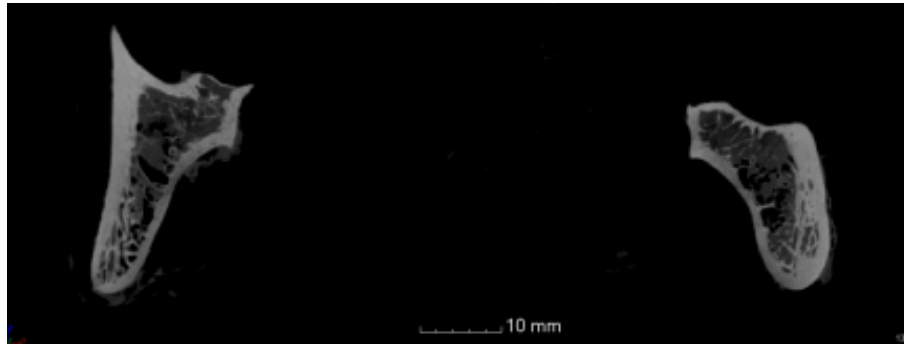


Figure 1 CT image of mandible. Notice how the right condyle is partly missing. The left condyle is completely missing and a part of the left ramus did not fit into the scan.

The 3D image was built out of slices of the mandible scanned with computer tomography (CT), which the CT software prepared and compiled into a volume of $30,383.8 \text{ mm}^3$. However the software is not able to distinguish the internal hollow cavities, which is why it was necessary to write a special program for this purpose.

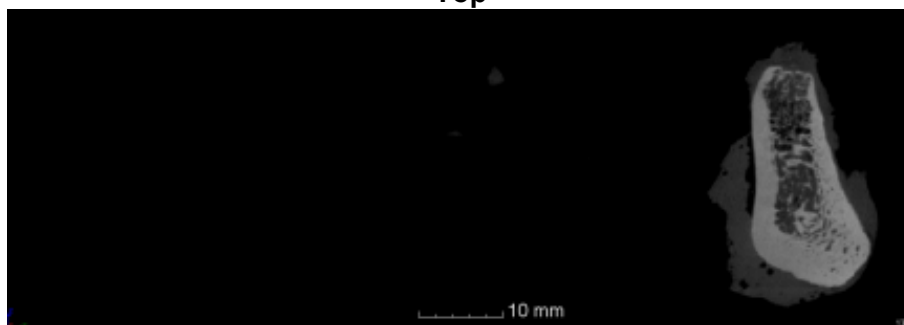
The scan was completed in three directions: from the front (front), from above (top), and from the side (right) (Fig. 2).



Front



Top



Right

Figure 2 The three directions: front (Front), from above (Top), and from the side (Right)

Since from the three scanning directions three different quantities of slices were made and the picture resolution introduces a certain level of error also, the sums made in each of the three directions give three different total volumes.

Measurement errors can result from the following (on the basis of errors in the CT equipment itself):

- Picture resolution

The lower the resolution, the more inexactly it composes the slice depicting the mandible, so the size of the pixels decides the precision with which it can take measurements from the scan.

- Pixel size inexactitude

The picture must be calibrated to the image processor (how many millimetres one pixel measures). The image processor then passes it on to the program, which completes the image processing. This is done on the basis of a reference measurement (an etalon) whose level of measurement precision is also a source of errors. Picture resolution also affects this reference measure, because the lower the resolution, the less exact is the possible measurement of the etalon length.

- Inexactitude in slice thickness

The program has to be given the thickness of a CT slice, with the help of which the program determines the volume. Imprecision attached to this dimension compounds with imprecision in the quantity of pixels in single slices. It is lucky that this value can be defined very exactly.

- Contour scanning error (based on greyness levels)

The program distinguishes the contours of the mandible from other parts of the picture slice by whether it is paler than a certain level of greyness. With changes in the greyness value used as a boundary value the discovered contour shifts and the value of the defined volume also.

- Defining pixels within the bone

The program must decide whether to depict a given pixel as part of the mandible or not, and an algorithm written earlier organises this decision. It is not always perfectly able to answer this question, since pixels occur in the scan image which either seem to be part of the mandible but are not, and vice versa.

- Errors calculating volume from the slices

From the diagram below it is easy to see that if there is a profile (left) which is assembled from slices (right) and if we notice that a given slice has a certain thickness then this can only approach the original profile (Fig. 3). Depending on how the profile 'thickens' or 'thins', this error reduces or increases the final volume.

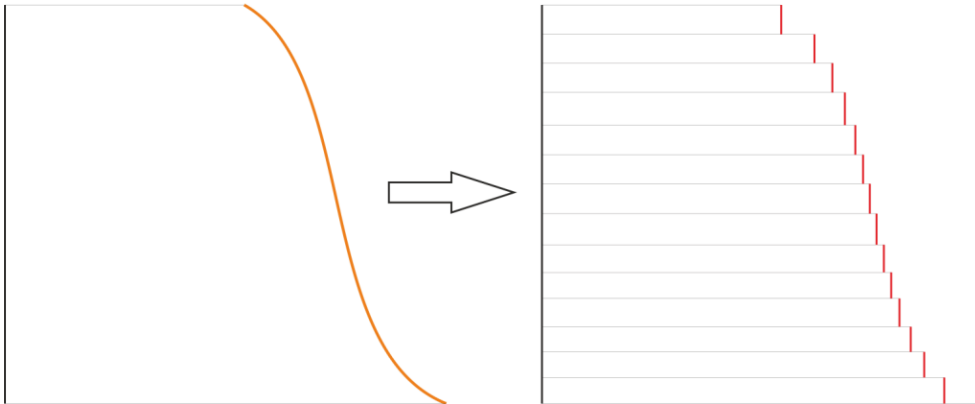


Figure 3 Shows how a theoretical curve is represented with a CT scan

Figure 4 shows how the CT scan carries out the slicing:

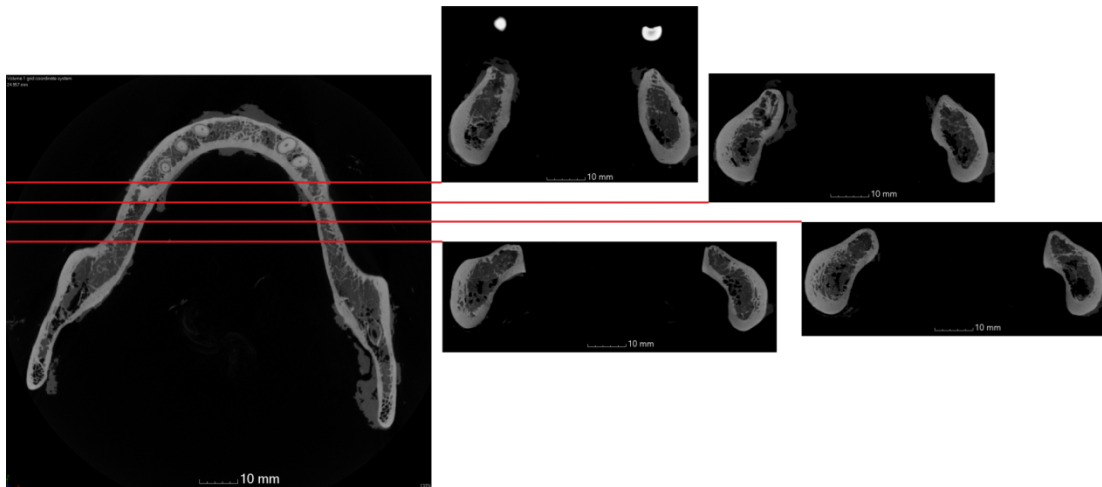
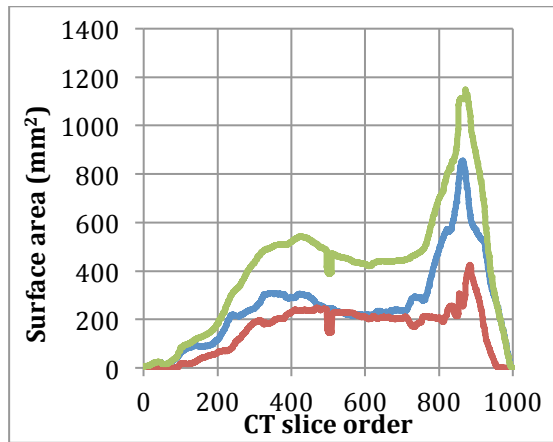
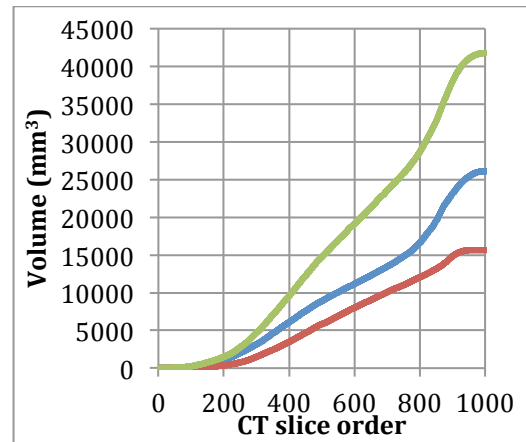


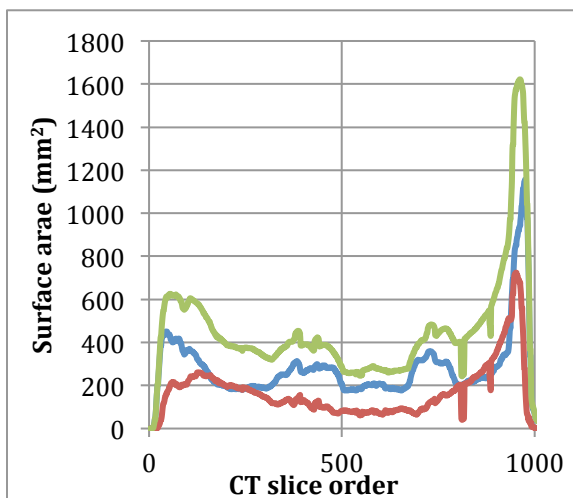
Figure 4 Shows four slices at different locations



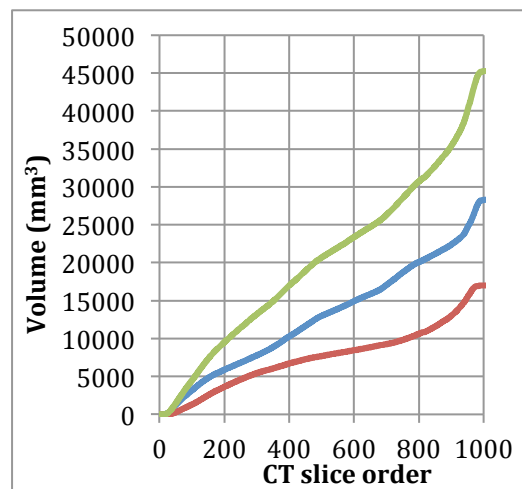
Surface area measured on frontal sections



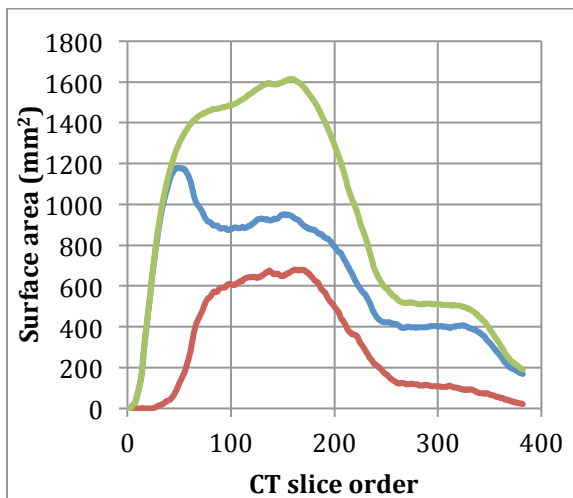
Compiled volume from the frontal sections



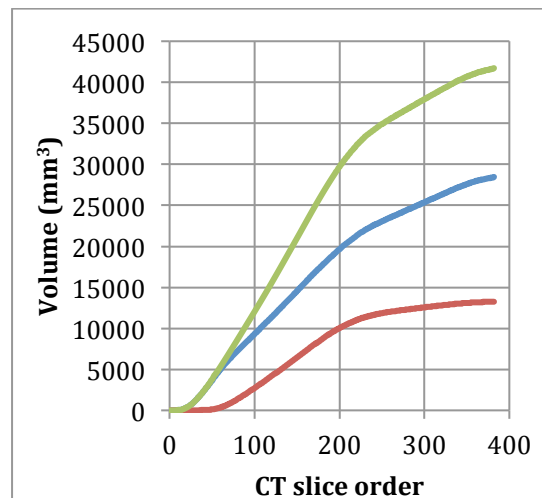
Surface area measured on the right sections



Compiled volume from the right sections



Surface area measured on the top section



Compiled volume from the top sections

Figure 5 The measured values of different sections; Legend: Blue line- Total bone, Red line- Hollow interior, Green line- Total mandibula

A common feature of the surface area diagrams for the region illustrated in Fig. 5 is that certain features of the 'total bone' curve appear shifted in the 'hollow interior' curve.

Volumes and their ratios:

Front: total volume = 41747.6 mm³; total bone volume=62.54%; hollow interior volume=37.46%

Right: total volume = 45300.3 mm³; total bone volume=62.54%; hollow interior volume=37.46%

Top: total volume = 41702.4 mm³; total bone volume=68.21%; hollow interior volume=31.79%

It is interesting to notice that the proportion of individual parts (%) changes less compared to the volumes (mm³). On the basis of scans from each direction, measured volume significantly deviates from total volumes defined by the CT scan. A probable explanation for this is that the CT program does not count the hollow spaces within the bone into the volume, but at the same time even added together each error is not enough to cause such a large deviation. On the basis of these, the total bone volume calculated by our program must be set with values that agree. Using these, the program calculated total bone volumes for each of the three directions.

Front: 26109.5 mm³

Right: 28329.8 mm³

Top: 28446.0 mm³

...as against the 30,383.8 mm³ measured by the CT scan, with which the values are comparable. The remaining deviation falls into a size ranking with the deviations among the individual directions. On the basis of these the images considered slice by slice underestimate the volume compared to the CT program.

It is important to note that the CT software also contains errors. Information saved by the CT in the .stl file format (stereo-lithographic file is treated as a prototype by the installations), which describes surfaces of a 3D object with the help of triangles, which are only an approximation to the true geometry. Furthermore the CT program is not able to distinguish dried soft tissues in the bone interior from bone itself, while our program can. This can explain overestimation of bone volume by the CT software.

6 Summary

My doctor and friend Miklos Fulop and I were in Nepal in March when he recommended Professor Lajos Patonay as someone to get in touch with if I wanted to work in the field of bone substitutes. Back in Budapest Miklos set up a meeting where he introduced me to Professor Patonay.

1. Handling of the mandible

The mandibles are fresh frozen mandibles from cadavers. The bones whenever they were not being scanned were kept in a cooler or a freezer. Each mandible was wrapped in nylon bags. We always used gloves when handling the mandible.

2. CT Machine, Scanning mode

From the very beginning I knew that I'd like to use a CT machine that had very high resolution. Although this CT machine was not suitable for scanning live patients, I realised it would give me the detail necessary for fuller analysis of trabecular bone. We had previously tested cone-beam and spiral computed tomography scanners before deciding that the more powerful machine in Gyor was the one we needed for this research.

3. Program development

The first programmer we worked with, Melinda Ban, was unfortunately unable to complete the project. This led to a search within the university for a second programmer who could pick up the project and make up for lost time. We finally found Zoltan Barta who was able to get a program up and running under the tight schedule that by then applied. The body of this thesis contains more detail of the error-checking and graphics handling that was necessary to make the visualisation software work compatibly with the output from the Gyor CT scanner.

4. Further test measurements

It was not possible to scan the entire mandible in the Gyor machine due to size constraints, so the mandible was scanned without the ramus and the condyle. Further test measurements and calibrations with an extra set of five human mandibles to refine the software will be possible once it can be exported from the machine it currently works on.

5. Further plans, conclusions

Once the program works successfully on other computers, we will be able to move ahead with tests on further human jawbones in order to improve error-handling and test for inconsistencies in the data. Due to the limited size of the machine at Gyor, further scans will be made easier once the Anatomy, Histology, & Embryology Department at Semmelweis University, Budapest cut each of these six mandibles into two pieces at the symphysis in the middle of the arch, enabling the whole of each half mandible to fit fully inside the scanner.

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