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**Towards a patient-specific vertebral finite element model using dual-energy radiography imaging to improve pedicle screw fixation: a feasibility study**

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Mémoire présenté en vue de l'obtention du diplôme de *Maîtrise ès sciences appliquées*

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présenté par **Carolina SOLORZANO BARRERA**

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## DEDICATION

*To my parents, for their unconditional support, even at a distance. Thank you.*

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## RÉSUMÉ

Environ 1,4 à 32 % des adultes de plus de 60 ans présentent une déformation de la colonne vertébrale, représentée par une courbure anormale d'une ou plusieurs sections de la colonne vertébrale. Pour traiter ce problème, on utilise une instrumentation avec des vis pédiculaires et des tiges pour réaligner et stabiliser la colonne vertébrale en vue d'une éventuelle fusion. Cependant, entre 0,8 et 27% des cas de fixation de vis pédiculaires échouent et sont principalement dus au mauvais alignement des trajectoires des vis et des déformations vertébrales, aux forces impliquées et aux propriétés mécaniques du tissu osseux.

Pour évaluer la fixation des vis pédiculaires, les tests d'arrachement (pullout) standards ont été utilisés dans les essais expérimentaux avec des échantillons cadavériques ou synthétiques. Cela limite toutefois la représentation des caractéristiques vertébrales humaines *in vivo*. La modélisation par éléments finis offre une solution alternative qui fournit une analyse biomécanique détaillée de la colonne vertébrale et peut simuler numériquement les tests d'arrachement pour évaluer la fixation des vis pédiculaires. Plusieurs études ont développé des modèles d'éléments finis (MEF) pour une seule vertèbre ou pour l'ensemble du rachis afin d'évaluer la force vertébrale, de prédire la fracture vertébrale et même la défaillance des vis. Ces modèles sont généralement conçus avec une géométrie générique et des propriétés mécaniques moyennes, généralement acquises à l'aide de modalités d'imagerie médicale telles que la tomodensitométrie (CT) ou la tomodensitométrie quantitative (qCT). Les propriétés spécifiques au patient peuvent être obtenues via ces modalités mais imposent un risque élevé d'exposition à la radiation ionisante pour le patient, ce qui limite leur utilisation.

Une grande variabilité de la densité osseuse a été observée dans l'os trabéculaire vertébral. La densité minérale osseuse semble être plus élevée dans les régions périphériques, tandis que les régions centrales présentent des valeurs plus faibles. Étant donné que la qualité de l'os varie considérablement d'une région vertébrale à l'autre et d'un individu à l'autre, le concept de modélisation spécifique des propriétés de l'os au patient a suscité un intérêt croissant pour la modélisation par éléments finis.

Un nouveau système d'imagerie à faible dose est présenté dans ce projet et a la capacité de fournir des radiographies bi-planaires (latérales et frontales) à double énergie (DE) qui sont acquises

simultanément sur un patient debout. Un module de double-énergie permet d'analyser la densité osseuse des vertèbres car elle calibre les radiographies en fonction de la densité de l'hydroxyapatite (HA). Ainsi, l'objectif de ce projet de recherche est de développer et de valider la faisabilité de l'intégration des propriétés mécaniques du tissu osseux spécifiques au patient en utilisant la radiographie à double énergie dans un MEF vertébral 3D pour améliorer la fixation des vis pédiculaires.

Un simulateur d'images fourni par la compagnie du système d'imagerie a été utilisé pour générer des radiographies bi-planaires, afin de travailler dans un environnement contrôlé. À l'aide d'un cas d'essai d'un scanner (CT) de patient provenant d'une base de données en libre accès, le simulateur d'images a généré des radiographies bi-planaires calibrées en polyméthacrylate de méthyle (PMMA) et en aluminium pour simuler respectivement les tissus mous et osseux, ainsi que des radiographies calibrées en HA pour simuler la densité minérale osseuse. Par conséquent, les valeurs de pixels des images ont été calibrées en  $\text{g/cm}^2$ .

Quatre MEFs isotropes de la 3e vertèbre lombaire (L3) ont été créés avec deux distributions différentes de l'os trabéculaire dérivées des radiographies DE ou de la densité minérale osseuse trabéculaire publiée dans la littérature : 1) moyenne (homogène) et 2) moyenne sur de petites régions d'intérêt (hétérogène). Cette dernière permet une visualisation individuelle des différentes sous-régions du corps vertébral et des éléments postérieurs, ainsi que des régions pédiculaires. Des mesures géométriques ont permis d'estimer la densité minérale osseuse volumétrique (vBMD) pour chaque région de la vertèbre. Après avoir évalué plusieurs relations mathématiques qui relient le module d'Young et la vBMD, l'équation de puissance de Keller et al., (1994) a été sélectionnée. D'autres propriétés mécaniques telles que la limite d'élasticité ou le coefficient de Poisson ont été obtenues à partir d'études antérieures sur des tests expérimentaux. La simulation de l'arrachement de la vis pédiculaire a été réalisée sur les quatre modèles où la vis était placée dans le pédicule droit. La distribution de la contrainte interne maximale, la rigidité initiale de l'interface os-vis et la force d'arrachement maximale ont été calculées et comparées entre les modèles.

Les résultats montrent que les modèles dont les propriétés sont dérivées des radiographies DE, comparés aux modèles de référence, augmentent respectivement la rigidité de l'interface os-vis sur le modèle homogène (5262 vs. 2232 N/mm) et le modèle hétérogène (4830 vs. 2314 N/mm). La force d'arrachement maximale augmente également pour le modèle homogène (418 vs. 298 N) et

hétérogène (511 vs. 371 N). De plus, une distribution des contraintes plus importante a été observée autour des filets des vis sur les modèles dont les propriétés sont dérivées des radiographies DE.

Les éléments postérieurs, les pédicules et la région postérieure du corps vertébral ont présenté une rigidité et une force d'arrachement maximale plus élevées sur les modèles hétérogènes que sur les modèles homogènes. Ces résultats sont attribués aux sous-régions postérieures du corps vertébral qui offrent une meilleure résistance au premier quart de la longueur de la vis pédiculaire pendant l'arrachement simulé. Cela peut être confirmé également par les valeurs de contrainte plus faibles trouvées autour des filets de vis sur le modèle hétérogène avec les propriétés dérivées des radiographies DE. Tous les résultats se situaient dans un intervalle acceptable quand ils ont été comparés avec des études expérimentales et numériques.

L'intégration des propriétés mécaniques spécifiques au patient dans un MEF vertébral avec une distribution hétérogène permet une perspective réaliste pour la planification de la chirurgie orthopédique par rapport aux résultats autrement sous-estimés dans une distribution homogène.

Le nouveau système d'imagerie à faible dose a l'avantage de fournir des radiographies calibrées en densité de HA permettant une quantification détaillée des propriétés mécaniques de l'os vertébral. Les recherches futures devraient se concentrer sur l'évaluation de la faisabilité du système d'imagerie sur d'autres régions du corps, comme le bassin ou les membres. Des algorithmes automatiques permettant un calcul rapide et précis de la densité minérale osseuse à partir de radiographies spécifiques au patient fourniraient de meilleurs résultats à intégrer dans les modèles numériques.

## ABSTRACT

Around 1.4 to 32% of adults over the age of 60 will experience a spine deformity, which is represented by an abnormal curvature in one or more sections of the vertebral column. When treating this issue, instrumentation with pedicle screws and rods are used to realign and stabilize the spine, in order to lead to fusion. However, between 0.8 to 27% of the cases of pedicle screw fixation fail and are mainly associated with the screw trajectory and vertebra deformity, the forces involved and the mechanical properties of the bone tissue.

To evaluate the fixation of pedicle screws, standard pullout testing is used in experimental testing with cadaveric or synthetic samples. This, however, limits the representation of *in vivo* human vertebral characteristics. Finite element modeling offers an alternative solution that provides detailed biomechanical analysis of the spine and can numerically simulate pullout tests to evaluate pedicle screw fixation. Several studies have developed single vertebra or full spine finite element models (FEMs) to evaluate vertebral strength, predict vertebral fracture and even screw failure. These models are generally designed with a generic geometry and average mechanical properties, generally acquired using medical imaging modalities such as computed tomography (CT) or quantitative computed tomography (qCT). Patient-specific properties can be obtained via these modalities but impose a high risk of ionizing radiation exposure to the patient, limiting their use.

A great variability of bone density has been observed in the trabecular vertebral bone. Bone mineral density seems to be higher in the peripheral regions, whereas the central regions present lower values. Because bone quality greatly varies between the vertebral region and between individuals, the concept of patient-specific modeling of bone properties has grown interest in finite element modeling.

A new low-dose imaging system is presented in this project and has the capacity of providing dual-energy (DE) bi-planar (lateral and frontal) radiographs, which are acquired simultaneously on a standing patient. A dual-energy modality allows the analysis of bone density of the vertebrae as it calibrates the radiographs accordingly with the density of hydroxyapatite (HA). Thus, the objective of this research project is to develop and validate the feasibility of integrating patient-specific mechanical properties of the bone tissue using dual-energy radiography in a 3D vertebral FEM to improve pedicle screw fixation.

An image simulator provided by the company of the imaging system was used to generate bi-planar radiographs, in order to work in a controlled environment. Using a test case of a patient CT scan from an open access database, the image simulator generated bi-planar polymethyl-methacrylate (PMMA)- and aluminum-calibrated radiographs to simulate soft and bone tissue, respectively, as well as HA-calibrated radiographs to simulate bone mineral density. Therefore, pixels values from the images were calibrated in  $\text{g/cm}^2$ .

Four isotropic FEMs of the 3<sup>rd</sup> lumbar (L3) vertebra were created with two different trabecular bone distributions derived from the DE radiographs or from published trabecular bone mineral densities: 1) averaged (homogeneous) and 2) averaged over small regions of interest (heterogeneous). The latter allows an individual visualization of the different subregions of the vertebral body and the posterior elements, as well as of the pedicle regions. Geometrical measurements allowed the estimation of volumetric bone mineral density (vBMD) for each region of the vertebra. After evaluating several mathematical relationships that relate the Young's modulus and the vBMD, the power-law equation of Keller et al., (1994) was selected. Other mechanical properties such as the yield stress or Poisson's ratio were obtained from previous studies on experimental tests. Pedicle screw pullout simulation was performed on the four models in which the screw was placed in right pedicle. The internal maximum stress distribution, the bone-screw interface initial stiffness and the peak pullout force were calculated and compared between the models.

Results showed that models with properties derived from DE radiographs, when compared to the reference models, respectively increase the bone-screw interface stiffness on the homogeneous (5262 vs. 2232 N/mm) and the heterogeneous (4830 vs. 2314 N/mm) models. The peak pullout force also increases for the homogeneous (418 vs. 298 N) and heterogeneous (511 vs. 371 N) models. Additionally, a higher stress distribution was observed around the screw threads on the models with properties derived from DE radiographs.

The posterior elements, the pedicles and the posterior regions of the vertebral body, reported higher stiffness and peak pullout force on the heterogeneous models compared to the homogeneous models. These results are attributed to the posterior subregions of the vertebral body which provide better resistance at the first quarter of the pedicle screw length during simulated pullout. This can be confirmed as well with the lower stress values found around the screw threads on the

heterogeneous model with properties derived from DE radiographs. All results were within acceptable range when compared to experimental and numerical studies.

Integrating patient-specific mechanical properties in a vertebral FEM with a heterogeneous distribution allows a realistic perspective for orthopedical surgical planning to otherwise underestimated results in a homogeneous distribution.

The novel low-dose imaging system has the advantage of providing HA density-calibrated radiographs allowing detailed quantification of the mechanical properties of the vertebral bone. Further research should concentrate on evaluating the imaging system's feasibility on other regions of the body such as the pelvis or limbs. Automatic algorithms that allow fast and accurate calculation of the bone mineral density from patient-specific radiographs would provide better results to integrate into numerical models.

## TABLE OF CONTENTS

|                                                                             |      |
|-----------------------------------------------------------------------------|------|
| DEDICATION .....                                                            | III  |
| ACKNOWLEDGEMENTS .....                                                      | IV   |
| RÉSUMÉ.....                                                                 | VI   |
| ABSTRACT .....                                                              | IX   |
| TABLE OF CONTENTS .....                                                     | XII  |
| LIST OF TABLES .....                                                        | XV   |
| LIST OF FIGURES .....                                                       | XVII |
| LIST OF SYMBOLS AND ABBREVIATIONS.....                                      | XXI  |
| LIST OF APPENDICES .....                                                    | XXII |
| CHAPTER 1    INTRODUCTION.....                                              | 1    |
| CHAPTER 2    LITERATURE REVIEW.....                                         | 3    |
| 2.1    Descriptive anatomy of the human spine .....                         | 3    |
| 2.1.1    Anatomy of the spine .....                                         | 3    |
| 2.1.2    Anatomy of the vertebra.....                                       | 5    |
| 2.1.3    Bone composition.....                                              | 6    |
| 2.2    Vertebral mechanical properties.....                                 | 7    |
| 2.2.1    Bone mechanics.....                                                | 7    |
| 2.2.2    The distribution of trabecular bone mineral density .....          | 9    |
| 2.2.3    Relationships between density and rigidity .....                   | 11   |
| 2.2.4    Estimated mechanical properties of the vertebral bone.....         | 13   |
| 2.3    Pedicle screw fixation .....                                         | 15   |
| 2.4    Finite element modeling of the spine .....                           | 17   |
| 2.4.1    Quasi-static models for biomechanical investigation purposes ..... | 17   |

|                                                                                                                                                                   |                                                                         |    |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------|----|
| 2.4.2                                                                                                                                                             | FEM for pedicle screw fixation.....                                     | 20 |
| 2.4.3                                                                                                                                                             | FEM refinement using imaging modalities.....                            | 22 |
| 2.5                                                                                                                                                               | Principles of dual-energy imaging .....                                 | 24 |
| 2.5.1                                                                                                                                                             | Description of a novel imaging system with dual-energy radiography..... | 28 |
| CHAPTER 3 RESEARCH OBJECTIVES AND ORGANIZATION OF THE WORK .....                                                                                                  |                                                                         | 30 |
| 3.1                                                                                                                                                               | Objectives.....                                                         | 31 |
| 3.1.1                                                                                                                                                             | Specific objectives.....                                                | 31 |
| 3.2                                                                                                                                                               | Organization of the work.....                                           | 31 |
| 3.3                                                                                                                                                               | Methodology overview .....                                              | 32 |
| CHAPTER 4 ARTICLE 1: TOWARDS A PATIENT-SPECIFIC VERTEBRAL FINITE<br>ELEMENT MODEL USING DUAL-ENERGY RADIOGRAPHY IMAGING TO IMPROVE<br>PEDICLE SCREW FIXATION..... |                                                                         | 33 |
| 4.1                                                                                                                                                               | Presentation of the article.....                                        | 33 |
| 4.2                                                                                                                                                               | Abstract .....                                                          | 34 |
| 4.3                                                                                                                                                               | Introduction .....                                                      | 34 |
| 4.4                                                                                                                                                               | Methods .....                                                           | 36 |
| 4.4.1                                                                                                                                                             | Dual-energy radiographic images .....                                   | 36 |
| 4.4.2                                                                                                                                                             | Definition of the vertebral models.....                                 | 37 |
| 4.4.3                                                                                                                                                             | Estimation of volumetric bone mineral density .....                     | 37 |
| 4.4.4                                                                                                                                                             | Computation of the mechanical properties.....                           | 38 |
| 4.4.5                                                                                                                                                             | Vertebral finite element model.....                                     | 39 |
| 4.5                                                                                                                                                               | Results .....                                                           | 40 |
| 4.6                                                                                                                                                               | Discussion .....                                                        | 40 |
| 4.7                                                                                                                                                               | Conclusions .....                                                       | 42 |

|                                                                                                                                      |                                 |    |
|--------------------------------------------------------------------------------------------------------------------------------------|---------------------------------|----|
| 4.8                                                                                                                                  | Acknowledgements .....          | 42 |
| 4.9                                                                                                                                  | Conflict of interests .....     | 42 |
| 4.10                                                                                                                                 | References .....                | 43 |
| 4.11                                                                                                                                 | Tables .....                    | 49 |
| 4.12                                                                                                                                 | Figures .....                   | 53 |
| CHAPTER 5 ESTABLISHING A FRAMEWORK FOR AN L3 VERTEBRAL FINITE<br>ELEMENT MODEL BASED ON PATIENT-SPECIFIC MECHANICAL PROPERTIES ..... |                                 | 60 |
| 5.1                                                                                                                                  | Methodology .....               | 61 |
| 5.2                                                                                                                                  | Results .....                   | 64 |
| 5.3                                                                                                                                  | Discussion and Conclusion ..... | 67 |
| CHAPTER 6 GENERAL DISCUSSION .....                                                                                                   |                                 | 68 |
| CHAPTER 7 CONCLUSION AND RECOMMENDATIONS .....                                                                                       |                                 | 72 |
| REFERENCES .....                                                                                                                     |                                 | 74 |
| APPENDICES .....                                                                                                                     |                                 | 82 |

## LIST OF TABLES

|                                                                                                                                                                                                                                                                                                                                 |    |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----|
| Table 2.1 Summary of the relationships for Young's modulus ( $E$ ) and bone density ( $\rho$ ) from experimental tests in the literature.....                                                                                                                                                                                   | 13 |
| Table 2.2 Summary of trabecular bone mechanical properties from different studies. ....                                                                                                                                                                                                                                         | 14 |
| Table 4.1 Estimated parameters from bi-planar dual-energy radiographs for the homogeneous model for a) the trabecular bone, and b) the cortical bone. The estimated volumetric bone mineral density is shown in bold.....                                                                                                       | 49 |
| Table 4.2 Computed parameters from bi-planar dual-energy radiographs for the heterogeneous vertebral model. The estimated volumetric bone mineral density is shown in bold as average vBMD (average from the lateral and posteroanterior view) .....                                                                            | 50 |
| Table 4.3 Mechanical properties computed from published data for the homogeneous and heterogeneous L3 vertebral reference model. Young's modulus was estimated using Equation 4.1. The remaining mechanical properties were obtained from previous published data .....                                                         | 51 |
| Table 4.4 Mechanical properties computed from dual-energy radiographs for the homogeneous and heterogeneous L3 vertebral model. Young's modulus was estimated using Equation 4.1. The remaining mechanical properties were set from published data ([8, 20, 33, 43]).....                                                       | 52 |
| Table 5.1 Description of the four models for the Young's modulus sensitivity test. ....                                                                                                                                                                                                                                         | 62 |
| Table 5.2 Mechanical properties for heterogeneous vertebral FEMs with different Young's moduli derived from equations in the literature. ....                                                                                                                                                                                   | 63 |
| Table 5.3 Results for pedicle screw pullout simulation for the four heterogeneous models with different estimated Young's moduli (HT001-HT004). ....                                                                                                                                                                            | 64 |
| Table 5.4 Correlation coefficients for pullout simulation parameters and models' average Young's modulus. ....                                                                                                                                                                                                                  | 66 |
| Table A.1 Geometrical measurements for the heterogeneous model trabecular bone subregions. Results highlighted in light grey were obtained from ImageJ measuring tool. Results highlighted in dark grey were obtained from Table A.2. Results in bold were the final estimated vBMD used in the methodology of this study. .... | 85 |

|                                                                                                                                                                                                                                                 |    |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----|
| Table A.2 Geometrical measurements for the samples taken on the trabecular bone from the PA view. Results highlighted in light grey were obtained from ImageJ measuring tool. ....                                                              | 86 |
| Table A.3 Geometrical measurements for the pedicle region. Results highlighted in light grey were obtained from ImageJ measuring tool. ....                                                                                                     | 87 |
| Table B.1 a) Volumetric bone mineral density from the work of Banse et al. (2001) which was used to b) corroborate and estimate the vBMD to use in the present work. Results in bold were used on the methodology presented in this study. .... | 89 |

## LIST OF FIGURES

- Figure 2.1 Anatomy of the full human spine. The five sections of cervical, thoracic, lumbar, sacral, and coccygeal vertebrae are shown in different colors. Adapted from “Human vertebra column”, by Luther Holden, 1887, Wikimedia Commons ([https://commons.wikimedia.org/wiki/File:Holden's\\_human\\_osteology\\_\(1899\)\\_-\\_Plt26.png](https://commons.wikimedia.org/wiki/File:Holden's_human_osteology_(1899)_-_Plt26.png)). In the public domain. ....4
- Figure 2.2 Anatomy of a human vertebra, viewed from a lateral and superior perspective. Adapted with permission from “Vertebra” by OlafJanssen, 2019, Wikimedia Commons ([https://commons.wikimedia.org/wiki/File:Vertebra\\_--\\_Smart-Servier.jpg](https://commons.wikimedia.org/wiki/File:Vertebra_--_Smart-Servier.jpg)). CC-BY-SA. ....6
- Figure 2.3 Stress and strain curves for cortical (left) and trabecular bone (right) in both compression and tension. From “The Bone Organ System: Form and Function”, by E.F. Morgan, G.L. Barnes and T.A. Einhorn, in R. Marcus and D. Feldman (Eds.), *Osteoporosis* (4<sup>th</sup> ed., p.20), 2013, Elsevier (<https://doi.org/10.1016/B978-0-12-415853-5.00001-7>). Copyright 2013 by Elsevier. Reproduced with permission. ....8
- Figure 2.4 a) Three types of anisotropy are typically encountered in bone tissue. From “The Bone Organ System: Form and Function”, by E.F. Morgan, G.L. Barnes and T.A. Einhorn, in R. Marcus and D. Feldman (Eds.), *Osteoporosis* (4<sup>th</sup> ed., p.21), 2013, Elsevier (<https://doi.org/10.1016/B978-0-12-415853-5.00001-7>). Copyright 2013 by Elsevier. Reproduced with permission. b) Vertebral trabecular bone architecture. Lines show the distribution orientation on different views of the vertebra. ....9
- Figure 2.5 Bone mineral density distribution reported in three studies. The scale ranges from very low to very high reported bone mineral density and shown in the trabecular bone area of the vertebral body. ....11
- Figure 2.6 a) Anatomy of a pedicle screw. b) Region in the pedicle where the pedicle screw is inserted. c) Types of pedicle screw trajectory. ....16
- Figure 2.7 The Spine Model for Safety and Surgery (SM2S). An example of the lumbar segment (L1-L5) is shown with different levels of detail. Vertebral ligaments are shown in orange and the intervertebral discs are shown in gray. ....19

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |    |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----|
| Figure 2.8 Pedicle screw finite element models presented in this section: a) Zhang et al. (2006), b) Liu et al. (2014), c) Xu et al. (2019), d) Abbeele et al. (2017), e) Bianco et al. (2017). Reproduced with permission.....                                                                                                                                                                                                                                                                                                                                                                                        | 22 |
| Figure 2.9 Mass attenuation coefficients for bone, soft and fat tissue. From “Skeletal Imaging”, by M.R. Allen and K. Krohn, in D.B. Burr and M.R. Allen (Eds.), <i>Basic and Applied Bone Biology</i> (1 <sup>st</sup> ed., p.93-113), 2014, Academic Press ( <a href="https://doi.org/10.1016/B978-0-12-416015-6.00005-8">https://doi.org/10.1016/B978-0-12-416015-6.00005-8</a> ). Copyright 2014 by Elsevier. Reproduced with permission.....                                                                                                                                                                      | 26 |
| Figure 3.1 Methodology overview for the present study. ....                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 32 |
| Figure 4.1 For the purpose of the feasibility study, the DE radiographic images were synthetically generated using available CT-scan from BioMedIA [22, 23], using the simulated image acquisition parameters shown above. Four sets of the DE radiographic images were generated to simulate the density of the acquired spine structures: 1) contour-enhanced image, 2) polymethyl methacrylate (PMMA) calibrated image (soft tissue), 3) aluminum (AL) calibrated image (bone tissue), and 4) hydroxyapatite (HA) density calibrated image .....                                                                    | 53 |
| Figure 4.2 Isotropic FEMs of L3. a) A homogeneous model with both cortical and trabecular bone elements. b) A heterogeneous model with trabecular elements divided into 8 subregions and a cortical bone layer. The trabecular bone subregions are named A through H as follows: A) trabecular superior-anterior, B) trabecular superior-central, C) trabecular superior-posterior, D) trabecular inferior-anterior, E) trabecular inferior-central, F) trabecular inferior-posterior, G) trabecular posterior elements, and H) trabecular pedicle region. c) Diagram of the four vertebral models of this study ..... | 54 |
| Figure 4.3 Mechanical properties of the four L3 vertebral models: a) homogeneous model from DE images, b) heterogeneous model from DE images, c) homogeneous reference model, and d) heterogeneous reference model. Values of volumetric bone mineral density ( $\rho$ , in g/cm <sup>3</sup> ) and Young’s modulus (E, in MPa) are shown over each region for trabecular and cortical bone                                                                                                                                                                                                                            | 55 |
| Figure 4.4 Meshed models with homogeneous and heterogeneous distribution with pedicle screw inserted in the right pedicle. Tetrahedral elements are seen in the trabecular bone surfaces. A closed-up view of the meshing between the screw model and the trabecular bone is displayed .....                                                                                                                                                                                                                                                                                                                           | 56 |

- Figure 4.5 Von Misses stress distribution in the trabecular bone after the pedicle screw pullout simulation for the four models. A color-coded legend shows the maximum stress presented on the model elements, red as the maximum value to blue as the lowest value. Images were captured for each model at their own peak pullout force, which is manifested at a different time for each one .....57
- Figure 4.6 Force-displacement curves for all vertebral models. Models with properties derived from DE images (light grey) reach peak force at a smaller displacement, when compared to the reference (dark grey). Homogeneous models (HM) are shown in bold and heterogeneous models (HT) are shown with dashed lines .....58
- Figure 4.7 Simulation results of pedicle screw pullout for the homogeneous and heterogeneous models with properties derived from DE images (light grey) and reference models (dark grey). The increase in peak pullout forces and initial stiffnesses are reported. There was no difference for the maximum stress values .....59
- Figure 5.1 Regression from mathematical equations for Young's modulus as a function of bone apparent density from four experimental published studies.....61
- Figure 5.2 Stress distribution around the trabecular bone on the vertebral FEMs with different Young's modulus. ....65
- Figure 5.3 Force-displacement curves for the four vertebral FEMs with different estimated Young's moduli.....66
- Figure A.1 Selected ROIs in the lateral view of the DE radiograph of the test case for L3. The labels 1 to 6 respectively correspond to the subregions defined in the left side of the figure. ....82
- Figure A.2 Representation of the measurements taken on the DE radiographs (LAT and PA) using ImageJ measurement tools. ....84
- Figure B.1 a) Anterior, posterior, and external cylindrical samples taken from thoracolumbar vertebrae bodies. b) Transverse cuts made on each cylindrical sample to measure vBMD from upper to lower sections. From “Inhomogeneity of human vertebral cancellous bone: systematic density and structure patterns inside the vertebral body”, by X. Banse, J.P.

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## LIST OF SYMBOLS AND ABBREVIATIONS

|      |                                             |
|------|---------------------------------------------|
| 3D   | Three-dimensional                           |
| AL   | Aluminum                                    |
| BMC  | Bone mineral content                        |
| BMD  | Bone mineral density                        |
| CT   | Computed tomography                         |
| DE   | Dual-energy                                 |
| DXA  | Dual-energy X-ray absorptiometry            |
| FEM  | Finite element model                        |
| HA   | Hydroxyapatite                              |
| LAT  | Lateral                                     |
| PA   | Posteroanterior                             |
| PMMA | Polymethyl-methacrylate                     |
| pQCT | Peripheral quantitative computed tomography |
| qCT  | Quantitative computed tomography            |
| ROI  | Region of interest                          |
| SM2S | Spine Model for Safety and Surgery          |
| vBMD | Volumetric bone mineral density             |

## LIST OF APPENDICES

|            |                                                                                                                       |    |
|------------|-----------------------------------------------------------------------------------------------------------------------|----|
| Appendix A | Manual estimation of patient-specific volumetric bone density from bi-planar bone-calibrated radiographic images..... | 82 |
| Appendix B | Estimation of volumetric bone mineral density for the reference vertebral model with published data.....              | 88 |

## CHAPTER 1 INTRODUCTION

Spine deformities can affect between 1.4 to 32% of adults aged over 60 years (Schwab et al., 2005). Non-surgical treatments are available, such as braces or exercises to reduce deformation and therefore reduce pain for the patients. In 35% of the cases, surgical intervention is needed to correct the spine and avoid further deformation and other health complications (Acaroglu et al., 2016).

The instrumentation used in these cases mainly consists of screws placed through the pedicles that are connected to rigid rods by means of large forces and moments, to realign the spine and correct the deformity, leading to its subsequent fusion. However, there is an incidence of 0.8 to 27% of reported cases for pedicle screw fixation failure (Bokov et al., 2019; Hicks et al., 2010). Bone quality, as well as the geometry of the vertebra play important roles for screw anchoring (Saman et al., 2013). Other factors include the screw dimension and trajectory when inserted (Bianco, R.-J. et al., 2017). Previous studies have shown the anisotropic behavior of the trabecular bone and have documented the different bone qualities of the vertebral regions (Augat et al., 1998; Inceoglu et al., 2005; Keaveny & Hayes, 1993; Nicholson et al., 1997). Bone quality also affects the fixation of the pedicle screws and their ability to withstand loads.

The performance of pedicle screws can be evaluated with pullout testing. This test is generally done on cadaveric vertebral or foam samples that represent the density of trabecular bone. However, it could limit the representation of *in vivo* vertebrae, as foams do not have the same rigidity and distribution characteristics, and as cadaveric samples often have a reduced bone quality. On the other hand, finite element modeling provides detailed biomechanical analysis of bone structures and allows simulating pullout testing to evaluate screw performance.

Medical imaging is used to define finite element models (FEMs) of the spine. The geometry and material properties of bone tissue are usually obtained with computed tomography (CT) (Fradet, L., Petit, et al., 2013; Liebschner et al., 2003; Xu et al., 2016) or quantitative computer tomography (qCT) (Buckley et al., 2007; Kopperdahl et al., 2002; Nazemi et al., 2016). The grey values found in the images can be calibrated with phantoms with known densities and mathematical associations are used to estimate mechanical properties. Even micro-computed tomography (micro-CT) could be used for a small segment of a cadaver spine to build a finite element model with detailed information at the tissue-level (Chen et al., 2017; Chevalier et al., 2018). Bi-planar dual energy X-

ray absorptiometry (DXA) was also used to build vertebral FEM using bi-planar radiographs to assess vertebral bone strength (Choisne et al., 2018).

Furthermore, most of these imaging technologies require large doses of ionizing radiation (Presciutti et al., 2014; Smith-Bindman et al., 2009) which limits their routine use in patients. Considering that spinal deformities also affect children and adolescents, a repeated exposure to ionizing radiation is harmful. Fortunately, other imaging technologies, which can reduce the radiation dose without compromising the quality of the radiographies, are emerging.

A novel imaging system is used in this project as a first-generation prototype with low-dose dual-energy technology. This system provides bi-planar radiographic images of a patient in a standing weight-bearing position allowing a full body scan. This technology uses the principles of dual-energy absorptiometry to visually separate bone and soft tissues of the body. In order to minimize the risk of radiation exposure, a technology of photon-counting detectors is incorporated in the system. This technology allows the acquisition of bone tissue calibrated images providing information of the bone density of the vertebrae and other bone structures. Since it is the aim of this project to analyze the influence of bone quality on pedicle screw fixation, bone mineral density can be used to estimate the mechanical properties of the bone.

The objective of this thesis project is to develop and evaluate the feasibility of integrating patient-specific mechanical properties of the bone using dual-energy radiography in a 3D vertebral finite element model to improve pedicle screw fixation modeling.

This thesis document is divided into seven chapters. Chapter 1 presents the introduction of the project. Chapter 2 presents the literature review on the necessary topics to introduce the context of the project. Chapter 3 presents the rationale and objectives of the project. Chapter 4 presents the methodology of the project and its results in the form of a research article. Chapter 5 presents complementary results of defining a framework for the vertebral FEM using dual-energy radiography. Finally, Chapters 6 and 7 present a general discussion and conclusions of the project, respectively.

## **CHAPTER 2      LITERATURE REVIEW**

### **2.1 Descriptive anatomy of the human spine**

#### **2.1.1 Anatomy of the spine**

The vertebral column, a central axis that supports the limbs and skull, is generally composed of 33 vertebrae arranged longitudinally from the head to the pelvis. The spine is divided into 5 sections: the cervical, thoracic, lumbar, sacral, and coccygeal sections (Figure 2.1). There are 7 cervical vertebrae (C1 – C7), which give support and movement to the head and neck. The thoracic section consists of 12 thoracic vertebrae (T1 – T12) and hold in place the thoracic cage by being attached to the ribs. Five lumbar vertebrae (L1 – L5) in the lumbar section give support to the lower back. Finally, there are generally five sacral vertebrae and four coccygeal vertebrae, which are fused in the adult form. The first three sections are known as the true (or movable) vertebrae as they allow flexibility to the body. The sacral and coccygeal vertebrae are considered false vertebrae. In some cases, the number of vertebrae found in each section could vary (Gray & Lewis, 1918).

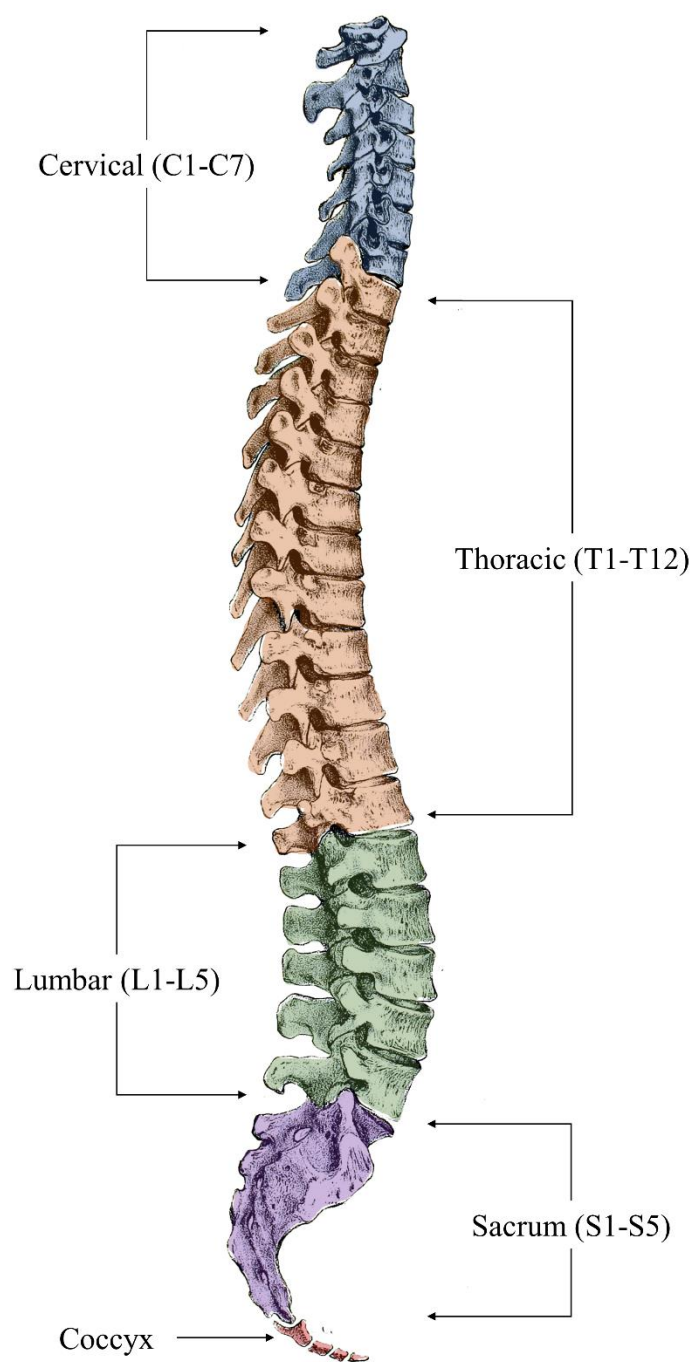


Figure 2.1 Anatomy of the full human spine. The five sections of cervical, thoracic, lumbar, sacral, and coccygeal vertebrae are shown in different colors. Adapted from “Human vertebra column”, by Luther Holden, 1887, Wikimedia Commons ([https://commons.wikimedia.org/wiki/File:Holden's\\_human\\_osteology\\_\(1899\)\\_-\\_Plt26.png](https://commons.wikimedia.org/wiki/File:Holden's_human_osteology_(1899)_-_Plt26.png)). In the public domain.

### **2.1.2 Anatomy of the vertebra**

A vertebra has two main sections: the body (anterior segment) and the vertebral arch (posterior segment). Both parts enclose a vertebral foramen through which the spinal cord passes. The body, also called the corpus vertebrae, is a cylindrical-shaped area mainly composed of cancellous bone and red bone marrow as well as a thin plate of compact bone. It is the largest part of the vertebra (Figure 2.2). The upper and lower surfaces are flattened, where the intervertebral disc rest and where the intervertebral fibrocartilages attach. In the anterior surface, there are small apertures for the passage of nutrient vessels.

The vertebral body attaches to the vertebral arch via the pedicles. These are two short and thick processes that extend from the posterolateral surfaces of the body. The laminae are two broad plates directed backward and medialward from the pedicles. The plates then fuse in the middle line to complete the posterior boundary of the vertebral foramen. From here, the spinous process extends backwards and downwards. It serves as an attachment to muscles and ligaments, and it is palpable in the back of a subject.

There are two other processes that grow from the junctions of the pedicles and laminae. These are called the articular processes and serve as an articulation to superior and inferior vertebra. In addition, at that same junction, the transverse processes extend at either side between the superior and inferior articular processes. Ligaments and muscles also attach to these processes (Saladin, 2012).

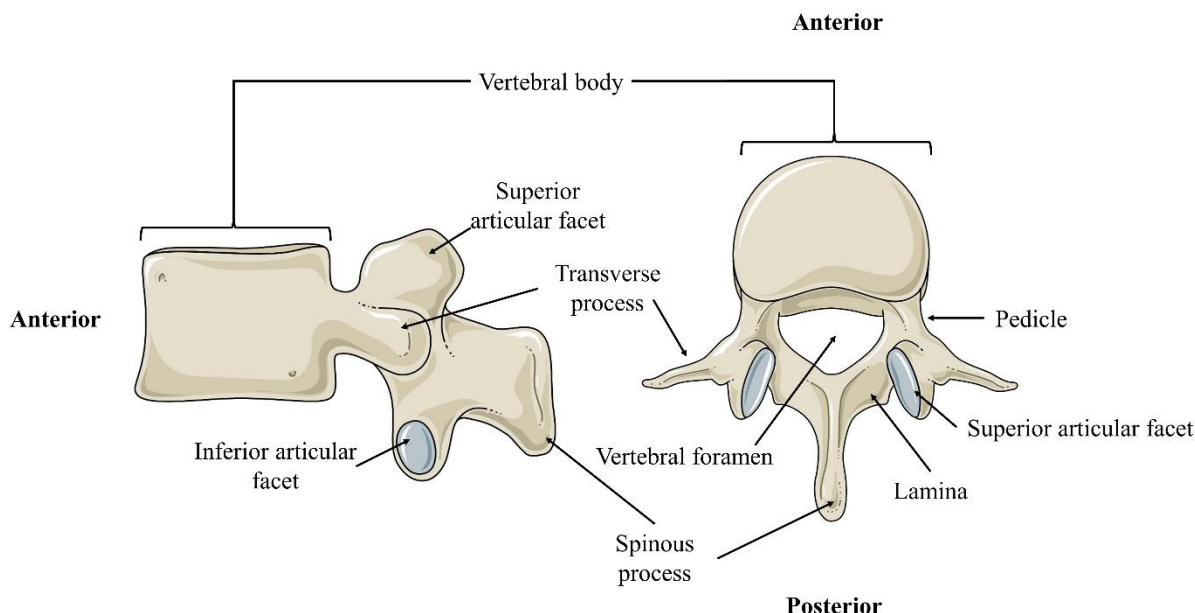


Figure 2.2 Anatomy of a human vertebra, viewed from a lateral and superior perspective. Adapted with permission from “Vertebra” by OlafJanssen, 2019, Wikimedia Commons ([https://commons.wikimedia.org/wiki/File:Vertebra\\_--\\_Smart-Servier.jpg](https://commons.wikimedia.org/wiki/File:Vertebra_--_Smart-Servier.jpg)). CC-BY-SA.

### 2.1.3 Bone composition

The bone as a tissue is one of the hardest structures of the body to support surrounding tissues but also possess a certain degree of elasticity. There are two kinds of bone: the cortical bone (compact or lamellar bone) and the trabecular bone (spongy or cancellous bone). The first surrounds the exterior of the bone and it is very dense. The latter is found on the inside of the bone, and it is more porous.

Cortical bone tissue is found in the external layers of the bone structure. It consists of concentric lamellae that are arranged around osteonic canals, which are organized to resist loads of bending or fracture and thus giving protection to the bone. Trabecular bone tissue is found in the inner layers of a bone. It consists of trabeculae, a tissue arranged as rods and plates that give this type of bone the appearance of a sponge. The empty spaces are permeated with bone marrow. The architecture of trabecular bone provides strength to the bone without compromising on the weight, as it is lighter than cortical bone. It is important to note that the trabeculae are not arranged

randomly but along the stress lines of the bone, which form accordingly to the forces applied during development (Gray & Lewis, 1918; Saladin, 2012).

## 2.2 Vertebral mechanical properties

### 2.2.1 Bone mechanics

Bone tissue provides mechanical support to body weight, protects organs, and is also subjected to many types of forces during different types of body movement. These mechanical forces shape the bone into remodeling during daily activity. Internal resistance, such as stress is distributed throughout the bone as it is dependent on force and area,  $\sigma = F/A$ , with units of Pascal (Pa).

Compression load is represented as a “pushing” force, where molecules in a material are squeezed together without creating a directed torque but reducing its size. Tension load, on the other hand, is the act to “pull apart” a material, which makes it to elongate in size. When two forces of opposite directions act in a right-angle, a shear load might cause the bone to fracture in two pieces. Other forces are created when a combination of loads is applied to a body. Torsion occurs when two rotating forces of opposite direction act on different points of a material whereas bending is the combination of compression on one side and tension on the other. The vertebrae are mainly subjected to compressive forces (Knudson, 2007).

Eventually, stresses could deform bone tissue resulting in strain  $\varepsilon = \frac{L-L_0}{L_0}$ , as the length measurements of the structure can change. A stress-strain curve of a material gives important information about its behavior to different loads. Figure 2.3 shows the stress-strain curve of cortical and trabecular bone tissue. The ascending slope of the curve represents the Young’s modulus of elasticity ( $E = \sigma/\varepsilon$ ) of a material, with units of Pa. This elasticity slope will display how much the material can withstand the load and return to its original shape with no change. Passing the elastic region, a material can have plastic behavior where deformations will be permanent. The limit within these regions is called the yield point and if a load is applied to a material that reaches through this point, it will not return to its original shape. Lastly, the fracture point represents the material’s failure (Culliane & Einhorn, 2002).

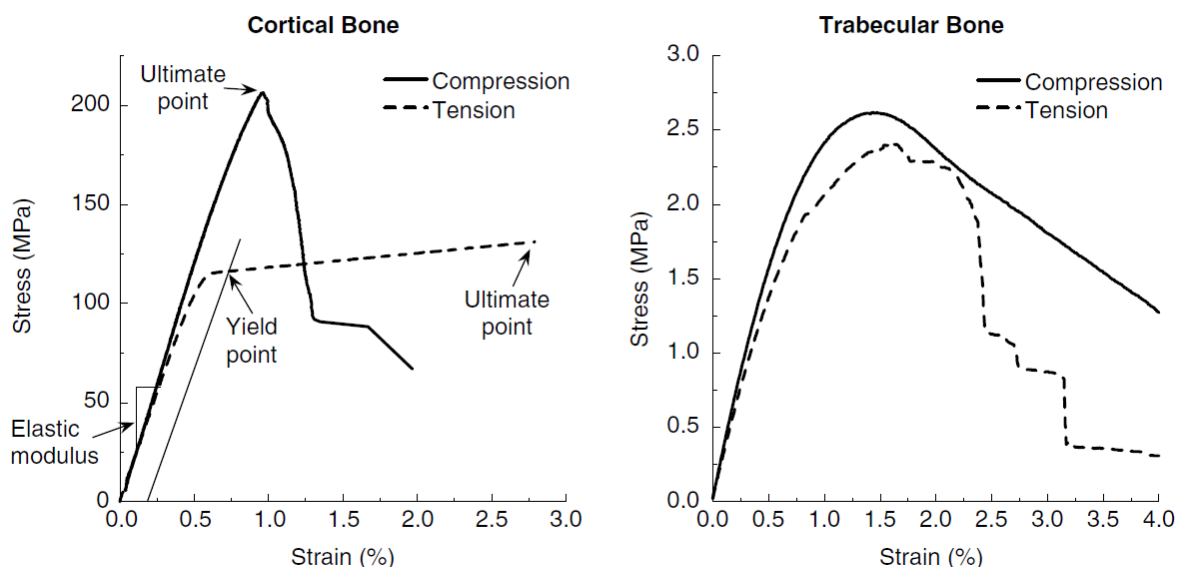


Figure 2.3 Stress and strain curves for cortical (left) and trabecular bone (right) in both compression and tension. From “The Bone Organ System: Form and Function”, by E.F. Morgan, G.L. Barnes and T.A. Einhorn, in R. Marcus and D. Feldman (Eds.), *Osteoporosis* (4<sup>th</sup> ed., p.20), 2013, Elsevier (<https://doi.org/10.1016/B978-0-12-415853-5.00001-7>). Copyright 2013 by Elsevier. Reproduced with permission.

Moreover, the mechanical properties of the bone vary according to the magnitude and the direction to the applied force. An ideal material would be homogeneous, i.e., an imaging phantom, and presenting isotropy as its mechanical behavior is the same regardless of load orientation. Bone tissue however presents anisotropic properties as their mechanical properties change according to the load direction (Culliane & Einhorn, 2002). The type of this anisotropy is considered orthotropic meaning the elastic modulus changes on three perpendicular directions (Figure 2.4a). Vertebral bone tissue for instance, presents greater anisotropy in the superior-inferior direction as that is the compressive force it receives from the full spine (Keaveny et al., 2001; Morgan et al., 2008). Trabecular bone architecture is therefore distributed along the stress lines that form from enduring daily activity (Figure 2.4b); an adaptability explained by Wolff’s law.

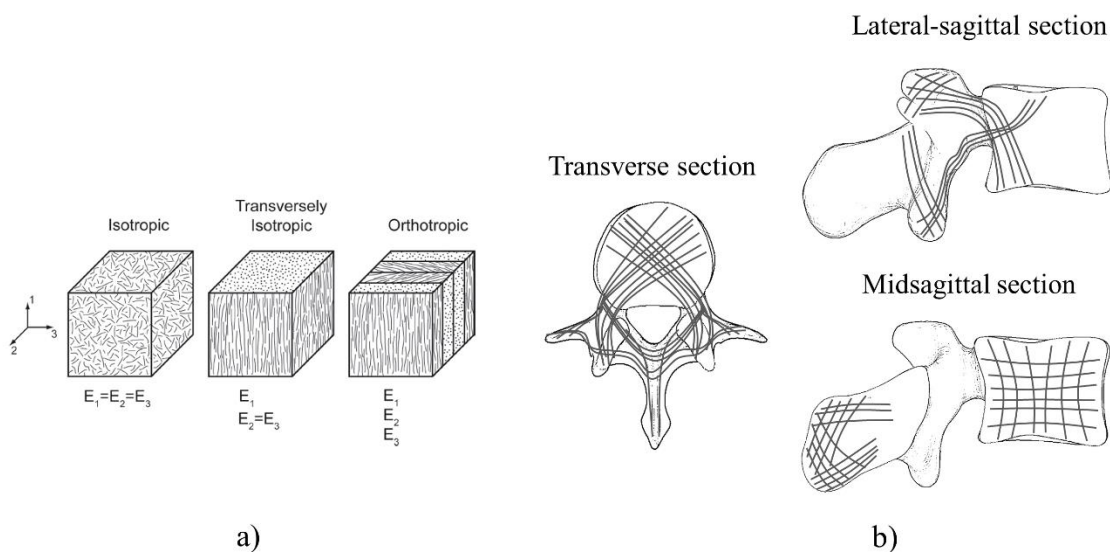


Figure 2.4 a) Three types of anisotropy are typically encountered in bone tissue. From “The Bone Organ System: Form and Function”, by E.F. Morgan, G.L. Barnes and T.A. Einhorn, in R. Marcus and D. Feldman (Eds.), *Osteoporosis* (4<sup>th</sup> ed., p.21), 2013, Elsevier (<https://doi.org/10.1016/B978-0-12-415853-5.00001-7>). Copyright 2013 by Elsevier. Reproduced with permission. b) Vertebral trabecular bone architecture. Lines show the distribution orientation on different views of the vertebra.

### 2.2.2 The distribution of trabecular bone mineral density

Bone density is an important property to consider regarding the mechanical properties of vertebral bone. Bone mineral density (BMD) is defined as the mass of bone mineral over the area of bone measured, given in  $\text{g}/\text{cm}^2$ . The reason to choose surface area is the convention of referring to BMD in the context of osteoporosis evaluation with the help of dual-energy absorptiometry, which generates planar images. However, one can refer to volumetric BMD, or vBMD, to the mass of bone mineral over a volume of bone tissue, given in  $\text{g}/\text{cm}^3$ .

The distribution of trabecular bone has been shown to differ between specific anatomical regions, where the trabeculae are more compacted or more spaced-out (Augat et al., 1998; Hayashi et al., 2011). This determines the BMD found in trabecular bone. As described previously, it presents

anisotropic mechanical properties. Furthermore, this means the distribution of its properties are not homogeneous, but heterogeneous.

The distribution of bone density in the trabecular vertebral bone is not uniform and some regions are denser than others. Depending on the loading that the bone sustains throughout a lifetime, the peripheral regions of the vertebral body have a different mechanical distribution than the central region (Figure 2.5). Banse et al. (2001) discussed the heterogeneity found in vertebral trabecular bone assessing 100 cylindrical samples of 17 thoracolumbar vertebral bodies (Banse et al., 2001). Additional four slices from top to bottom were done with peripheral qCT (pQCT). Results showed that the posterior cores of the vertebral bodies presented higher density values than the anterior cores. The upper half of the vertebral body had the lowest density values compared to the lower half. The external samples (outer region of the vertebral body) presented heterogeneity as well as the posterior samples when compared to the anterior samples, which were vertically homogeneous. The lowest density values were found on the superior and external part of the lumbar vertebra. On the other hand, the highest values were on the lower half and posterior part of the thoracolumbar vertebra.

Other studies have reported similar density distribution patterns with DXA (Briggs et al., 2006) and micro-CT (Fradet, Leo, 2014; Fradet, L., Vachon, et al., 2013), clearly showing that the vertebral trabecular bone is heterogeneous. Overall, the anatomical sites of the vertebra presenting high trabecular bone density are the posterior sites, specifically the inferior-posterior sites (Figure 2.5). High trabecular bone density values were also reported for the pedicles (Inceoglu et al., 2005). Their morphology and anatomy provide an ideal implantation region for surgical screws as it allows a load distribution between the vertebral body and the posterior elements along with the posterior ligaments of the spine. Thus, the trabecular bone of the vertebrae has a distribution of bone density throughout its vertebral body and posterior elements, including the pedicles, caused by the adaptation of compressive forces and thus reflects a heterogeneous distribution of its mechanical properties.

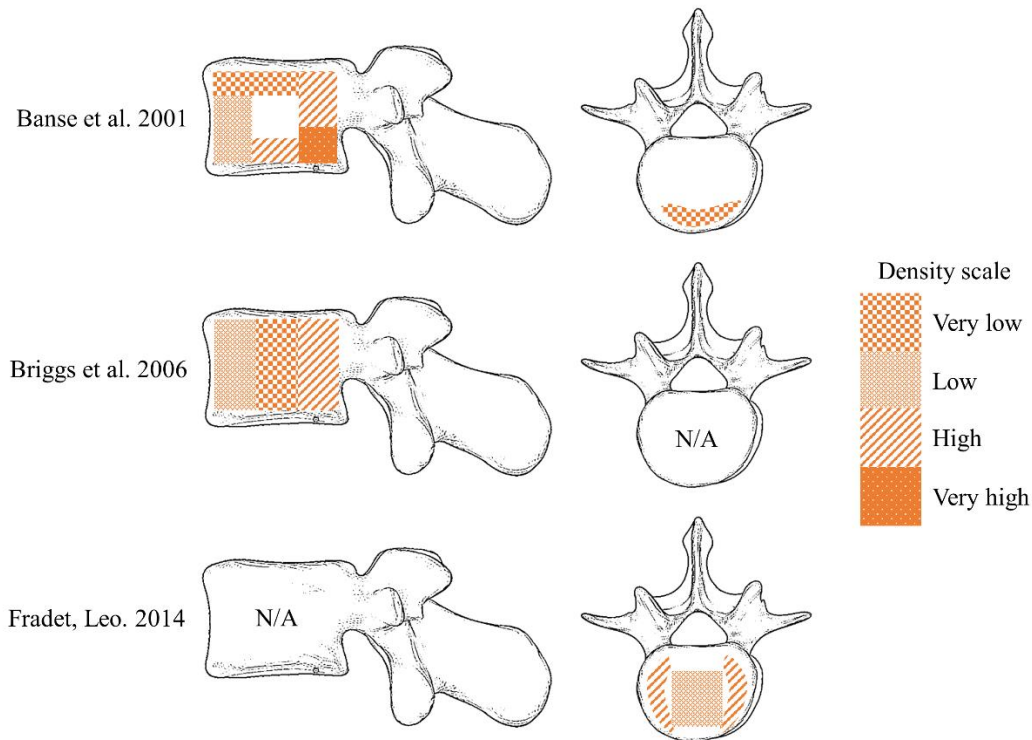


Figure 2.5 Bone mineral density distribution reported in three studies. The scale ranges from very low to very high reported bone mineral density and shown in the trabecular bone area of the vertebral body.

### 2.2.3 Relationships between density and rigidity

The elastic modulus (Young's modulus or rigidity) and the apparent density of trabecular bone are physically interdependent. The form of their relationship however remains to be precisely determined, as trabecular bone, and therefore the elastic modulus, are anisotropic. Many studies have done experimental testing on thoracolumbar and lumbar human vertebrae to establish said relationships (Helgason et al., 2008). The summary of some studies considered for this project is shown in Table 2.1 and described as follows:

- An equation from Keller (1994) was obtained through 199 vertebral samples from adult lumbar vertebrae aged 70, 77 and 78 years old (no specification of vertebral sections) (Keller, 1994). Loads were applied at the superior-inferior direction with crosshead speed

of 5 mm/min and average strain rate of  $0.01 \text{ s}^{-1}$ . The apparent ash and dried densities of fat free bone were estimated experimentally. Linear and power predictions for Young's modulus as a function of bone density were estimated. The resulted apparent ash density for lumbar vertebrae ranged between 0.028 and  $0.182 \text{ g/cm}^3$ .

- An equation from Keaveny et al. (1997) was obtained through 9 final vertebral samples from adult lumbar vertebrae aged 46 to 91 years old (no specification of vertebral sections) (Keaveny et al., 1997). Uniaxial compression loads were applied at a strain rate of  $0.005 \text{ s}^{-1}$  for 10 cycles, 0 to 0.3% strain. Apparent density was measured and ranged between 0.09 to  $0.28 \text{ g/cm}^3$ . Finally, linear predictions for Young's modulus were estimated.
- An equation from Kopperdahl & Keaveny (1998) was obtained with 44 vertebral samples from adult thoracolumbar vertebrae (T10-L4) with mean age of 54 (Kopperdahl & Keaveny, 1998). Non-destructive uniaxial compressive load was applied with  $\pm 0.1\%$  strain at  $0.5\% \text{ strain s}^{-1}$  and destructively to 3% strain. The wet apparent density was measured experimentally and ranged from 0.11 to  $0.26 \text{ g/cm}^3$ . Linear and power-law regressions were measured for Young's modulus, as well as yield strain (%), ultimate strain (%), yield stress (MPa) and ultimate stress (MPa).
- An equation from Morgan et al. (2003) was obtained with 61 thoracolumbar vertebral samples (T10-L5) from 61 donors with mean age of 62 (Morgan et al., 2003). Compressive tests for 30 samples were done with a load to 0.1% at  $0.5\% \text{ strain s}^{-1}$  just to the yield point. Apparent density was determined with the Archimedes' principle. Finally, power-law regressions for the Young's modulus were estimated.

From these and other studies (Helgason et al., 2008), the bone density found in a specific anatomical site (femur, vertebrae, proximal tibia, greater trochanter, etc.) has a limited range. Thus, as concluded by Keaveny et al. (2001), the differences found between linear or power-law mathematical relationships for elastic modulus and bone density are trivial (Keaveny et al., 2001). Additionally, relationships between bone density and other mechanical properties have been studied, as is for yield stress and strain (Bevill et al., 2009; Kopperdahl & Keaveny, 1998), and ultimate strength (Fleps et al., 2020).

Table 2.1 Summary of the relationships for Young's modulus ( $E$ ) and bone density ( $\rho$ ) from experimental tests in the literature.

| Authors                      | Age (mean) | Vertebral sample | Density range (g/cm <sup>3</sup> ) | $E$ (GPa)               | $r^2$ | n   |
|------------------------------|------------|------------------|------------------------------------|-------------------------|-------|-----|
| (Keller, 1994)               | 70, 77, 78 | Lumbar           | 0.028 – 0.182                      | $E = 1.89\rho^{1.92}$   | 0.702 | 199 |
| (Keaveny et al., 1997)       | 46-91 (NA) | Lumbar           | 0.09 – 0.28                        | $E = 1.540\rho - 0.058$ | 0.64  | 9   |
| (Kopperdahl & Keaveny, 1998) | 32-65 (54) | T10-L4           | 0.11 – 0.27                        | $E = 2.1\rho - 0.08$    | 0.61  | 44  |
| (Morgan et al., 2003)        | 20-90 (62) | T10-L5           | 0.11 – 0.35                        | $E = 4.730\rho^{1.56}$  | 0.73  | 61  |

## 2.2.4 Estimated mechanical properties of the vertebral bone

Experimental studies have reported the estimated values for trabecular bone mechanical properties. These properties can be later used to assume material behavior in finite element modeling. In these studies, different anatomical structures were experimentally tested to obtain a range of estimates of bone mineral density, Young's modulus, Poisson's ratio, yield stress and strain, and ultimate stress and strength. A summary of these value ranges is reported in Table 2.2.

Table 2.2 Summary of trabecular bone mechanical properties from different studies.

| Anatomical site | Bone mineral density (g/cm <sup>3</sup> ) | Young's modulus (MPa) | Poisson's ratio                | Yield strain (%) | Yield stress (MPa) | Ultimate stress (MPa) | Ultimate strength (MPa) | References                     |
|-----------------|-------------------------------------------|-----------------------|--------------------------------|------------------|--------------------|-----------------------|-------------------------|--------------------------------|
| N/A             | 0.05 - 0.10                               |                       | 0.3                            | 1.59 - 2.45      |                    |                       |                         | (Keaveny & Hayes, 1993)        |
| Tibiae          | 1.74 - 1.952                              | 14300 - 21100         | -                              | -                | -                  | -                     | -                       | (Snyder & Schneider, 1991)     |
| L2-L5           | -                                         | 90.46 - 139.1         | 0.03 - 0.1                     | -                | -                  | -                     | -                       | (Silva, A. M. H. et al., 2019) |
| T10-L4          | 0.11 - 0.26                               | 90 - 536              | -                              | 0.75 - 0.95      | 0.56 - 3.71        | 0.7 - 0.433           | -                       | (Kopperdahl & Keaveny, 1998)   |
| L3-L4           | 0.131 - 0.135                             | 53 - 73               | -                              | -                | -                  | -                     | 1.1 - 1.5               | (Augat et al., 1998)           |
| T10-L5          | 0.11 - 0.35                               | -                     | -                              | -                | -                  | -                     | -                       | (Morgan et al., 2003)          |
| T12-L4          | 0.46 - 0.71                               | -                     | -                              | -                | -                  | -                     | -                       | (Ouyang et al., 1997)          |
| Lumbar spine    | 0.09 - 0.28                               | -                     | -                              | -                | -                  | -                     | -                       | (Keaveny et al., 1997)         |
| Vertebral bone  | 0.028 - 0.182                             | 32 - 355              | -                              | -                | -                  | -                     | 0.045 - 0.161           | (Keller, 1994)                 |
| L3-L4           | -                                         | -                     | 0.034 - 0.754<br>0.031 - 0.571 | -                | -                  | -                     | -                       | (Yahia et al., 1988)           |

## 2.3 Pedicle screw fixation

Surgical intervention is required sometimes to treat spinal deformities. Pedicle screws help to stabilize the affected vertebral segment by either fusing or fixating vertebrae together (Jain et al., 2020). A pedicle screw consists of a metal screw with a head and a body either single or double threaded. The screw body shape can either be conical, with a smaller minor diameter, or cylindrical, where the shape remains the same throughout the screw length (Figure 2.6a). Generally, pedicle screws are made of stainless steel, titanium alloy, or CoCr (Shen et al., 2019). The diameter and length of the screw can widely vary between manufacturers and between its intended application, such as the disease treated, vertebral segment or vertebral bone quality.

Pedicle screws are inserted posteriorly through the pedicles of the vertebra and into the vertebral body (Figure 2.6b), whilst removing a layer of cortical bone. There are three types of trajectories used: anatomic, which aims the center of the vertebral body and avoids the cortical layer; straight forward, which aims the center of the superior vertebral endplate; and straight ahead, which is positioned in the most peripheral region of the pedicles and parallel to the superior vertebral endplate (Figure 2.6c). Each trajectory has a different purpose to maximize screw anchoring and the choice remains at the surgeon's discretion.

To evaluate the performance of a pedicle screw *ex vivo*, the standard pullout test is used (ASTM, 2017). This consists in applying an axial load on a pedicle screw that has been already inserted into a vertebral specimen or foam sample. A constant displacement rate is applied until the maximum force required to loosen up the screw is reached, which is called the pullout force. This allows reproducibility between tests and samples, but it is uncommonly used in a clinical setting (Shea et al., 2014). Screw anchoring can therefore be evaluated while considering different variables such as bone quality.

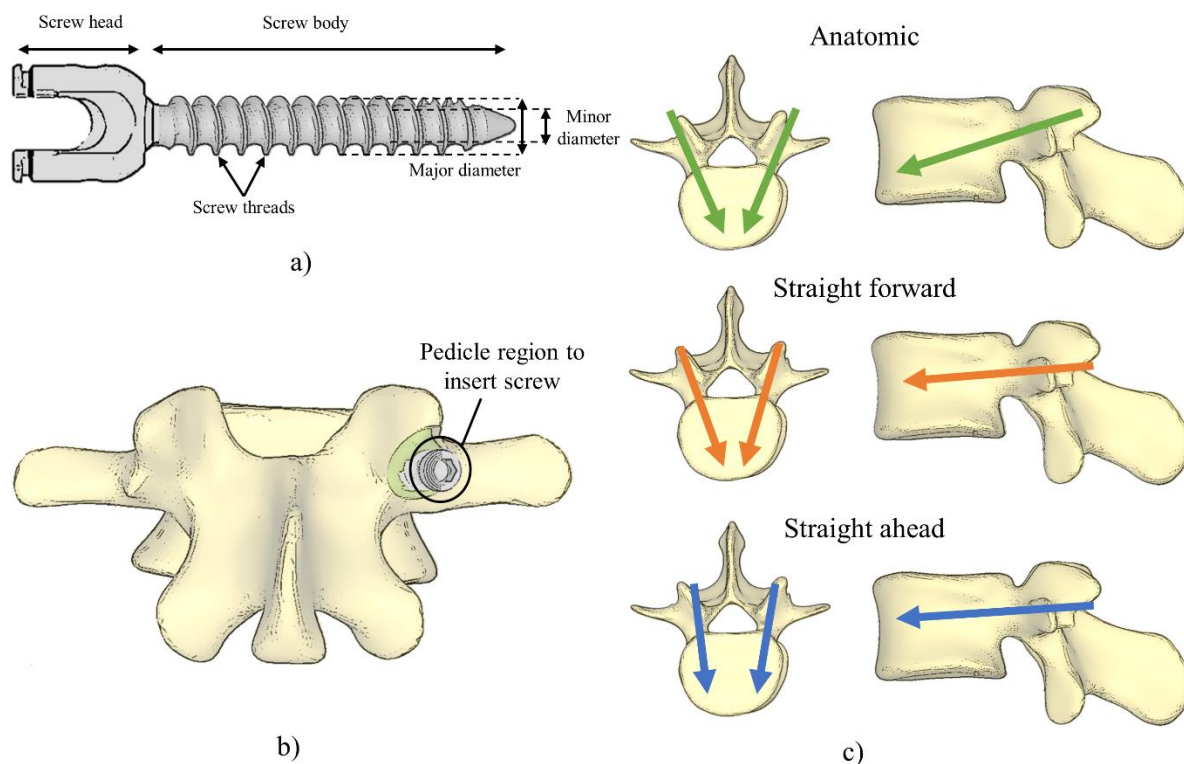


Figure 2.6 a) Anatomy of a pedicle screw. b) Region in the pedicle where the pedicle screw is inserted. c) Types of pedicle screw trajectory.

It has been reported that bone mineral density and its distribution are important factors that affect pedicle screw anchoring. Osteoporosis, for example, causes low bone mineral density affecting the trabecular bone more than the cortical bone. Surgical intervention is often also required for osteoporotic patients which challenges the planning of pedicle screw fixation. Lai et al. (2018) aimed to determine the ideal diameter size for pedicle screws in osteoporotic vertebrae comparing pullout and fatigue tests (Lai et al., 2018). Their results concluded that a smaller diameter (4.35 mm) could reduce the risk of pedicle breakage for poor bone quality. Shen et al. (2019) have reported the best design of pedicle screw depending on the bone quality and presented a double dual-threaded screw that is best for osteoporotic bone (Shen et al., 2019). Okuyama et al. (2010) presented that the range value of BMD of  $0.674 \pm 0.104$  g/cm<sup>2</sup> with dual-energy X-ray absorptiometry would have an increased risk for screw loosening, but did not present a biomechanical approach (Okuyama et al., 2001). Lastly, Weiser et al. (2017) determined with

fatigue tests that a BMD below  $0.8 \text{ g/cm}^3$  would present a risk in pedicle screw stabilization (Weiser et al., 2017). Also, that there is a correlation between BMD and pedicle screw stability.

Pedicle screw dimensions, trajectory, and position, as well as technique are additional factors that affect screw fixation. However, bone quality is related to screw anchoring as confirmed with the mentioned studies and thus should be considered in the evaluation of pedicle screw performance.

## **2.4 Finite element modeling of the spine**

### **2.4.1 Quasi-static models for biomechanical investigation purposes**

Numerical modeling allows the analysis for simulated scenarios on geometrical structures, such as the spine. Multi-body modeling presents a dynamic insight of rigid and flexible interconnected bodies, but do not allow a detailed analysis for geometrical deformation. Finite element modeling, on the other hand, has shown to be a better alternative for biomechanical simulation and analysis of complex geometries at a detailed level (Naoum et al., 2021). The model geometry is composed of elements that possess a system of equations allowing the resolution of a global problem into an approximate result. The system of equations is solved with differential equations that run iteratively and therefore increase computational time, depending on the size of the model's mesh, elements, and overall geometry. Material properties can be added to every component of the finite element model (FEM), such as in the case of a spine model, the cortical and trabecular bone, ligaments, and intervertebral discs.

Spine FEMs are usually created with imaging modalities such as CT scan (Guo & Li, 2019; Liebschner et al., 2003), by generating volumes of interest, or with X-ray, by generating reconstructions with stereoradiography (Choisne et al., 2018; Fougerson et al., 2018; Henao et al., 2015). The process to design a spine FEM is to create 3D surfaces of the vertebra following the geometry from CT scan or X-ray reconstruction. Then, modeling software creates a mesh around these surfaces to determine the elements within the model. The 3D elements can either be tetrahedral, pyramidal, triangular prisms or hexahedral shapes. Finally, some refinement is needed to establish good mesh quality around the structure. Material properties and boundary conditions for quasi-static loads can be later applied onto the model before the final simulation is launched (Palomar et al., 2008). As mentioned previously, depending on the number of elements, FEMs take

on long computational time to perform simulations, and even longer for a better-quality meshed geometry.

Quasi-static FEMs of the spine have been presented to assess problematics on vertebral strength, failure, or fracture. Silva et al. (1998) presented a CT-based FEM of the thoracolumbar spine (T11-L2) to evaluate the prediction of failure and fracture during compression loading (Silva, M. J. et al., 1998). Their model was based on 10 mm thick section cuts from the vertebral bodies, giving a total mesh size of 360 elements. Xu et al. (2016) presented a CT-based lumbar FEM from five subjects (Xu et al., 2016). The trabecular bone, a cortical shell layer with a 0.5 to 1 mm thickness distribution, endplates, cartilage joints and seven major ligaments were modeled. Mesh sensitivity, convergence, and validation with experimental data of the overall model were performed. A mesh with approximately 99,600 elements was considered to be stress-converged. Finally, this model proved to be valid and introduced its potential to be used in biomechanical analysis for clinical applications. Moreover, Dreischarf et al. (2014) assessed the high inter-subject variability of spine FEMs (Dreischarf et al., 2014). Their comparison with multiple spine FEMs from different research organizations demonstrated that a probabilistic approach of combined FEMs can be used as a predictive tool for lumbar biomechanical numerical analysis. This means that there is a high variability on the population spine characteristics that, even though proven experimentally (Hayashi et al., 2011; Limthongkul et al., 2010; Morales-Avalos et al., 2014; Singer et al., 1995), needs to be considered numerically for patient-specific usage (Garo, A. et al., 2009; Garo, Anaïs et al., 2011).

El-Rich et al. (2008 & 2009) developed a comprehensive model of the human spine for traumatic applications (El-Rich, Marwan et al., 2009; El-Rich, M. et al., 2008), which was extended later to the thoracolumbar spine (Fradet, L., Petit, et al., 2013). The model, called Spine Model for Safety and Surgery (SM2S), was developed within the framework of the iLabSpine International Laboratory, which is a collaboration between Polytechnique Montreal, CHU Sainte-Justine and the Laboratory of Applied Biomechanics of the University of Aix-Marseille and the University Gustave Eiffel, as well as several other institutions in Montreal and Marseille (Figure 2.7). The model was based on the reconstruction of a 32-year-old non-pathological Caucasian male in the 50th percentile using CT scan with 0.6 mm thick slices. The model includes bone structures divided into cortical and trabecular bone, ligaments, endplates, and intervertebral discs. The cortical bone

and endplates were modeled with shell elements, and the cancellous and posterior elements with solid elements. In the work of El-Rich, et al. (2008), a lumbar segment (L2-L3) was validated under quasi-static compression as well as with dynamic loading. Further studies have used the same model to evaluate vertebral fracture with compression, torsion and bending moments (Fradet, L., Petit, et al., 2013), high and low dynamic loading for spinal injury assessment (Garo, Anaïs, 2010; Wagnac et al., 2012), as well as pedicle screw fixation (Bianco, R.-J. et al., 2017; Bianco, R., 2015). The latter work is described in detail in section 2.4.2. of this thesis.

Wagnac et al. (2012) presented a lumbar FEM using the SM2S model in dynamic loading (Wagnac et al., 2012). The trabecular bone was divided into seven zones including the upper and lower regions of the vertebral body as well as anterior, middle, and posterior segments, and the posterior elements of the vertebrae. The BMD was included for each zone from the work of Zhao et al. (2009) (Zhao et al., 2009). The other mechanical properties of each trabecular bone zone were defined as isotropic and homogeneous, and no further specific studies were performed regarding these subdivisions.

Based on these various published studies, the SM2S model will be retrieved and adapted for the needs of the project.

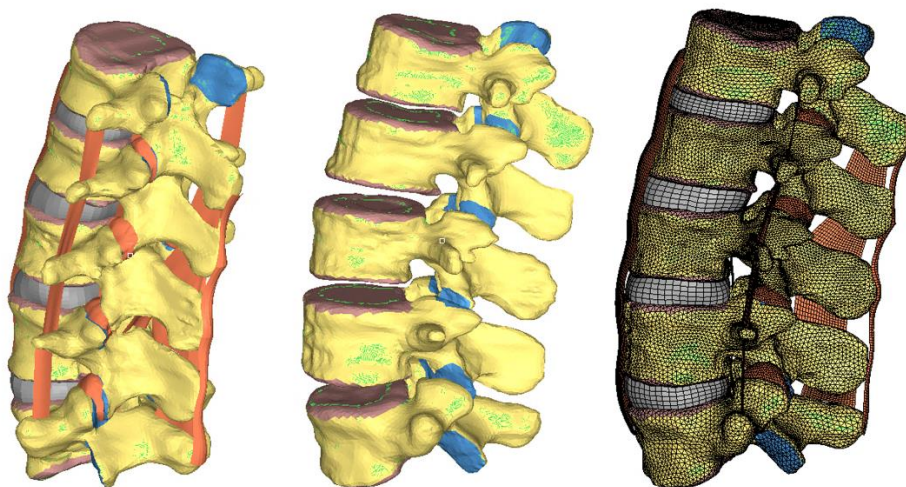


Figure 2.7 The Spine Model for Safety and Surgery (SM2S). An example of the lumbar segment (L1-L5) is shown with different levels of detail. Vertebral ligaments are shown in orange and the intervertebral discs are shown in gray.

### 2.4.2 FEM for pedicle screw fixation

Pedicle screw fixation has been evaluated with vertebral FEMs that either present a simple or realistic morphological geometry. Figure 2.8 shows the FEMs discussed in this section.

Liu et al. (2014) presented a finite element model of the pedicle to define effective fixation conditions when simulating pedicle screw pullout (Liu et al., 2014). The model of a CD Horizon legacy 6.5 x 40 mm pedicle screw was used, and the pedicle FEM was modeled as a cylindrical block of 18 mm x 4 mm. The model was compared to an experimental study with polyurethane foams of high (0.32 g/cm<sup>3</sup>) and low (0.16 g/cm<sup>3</sup>) densities, with consequently high (137.5 MPa) and low (23 MPa) Young's moduli. They concluded that there is an effective cylindrical region around the screw in the pedicle to resist pullout, with a high magnitude of stress in the region closest to the screw threads. Their goal was to suggest a region of interest for pedicle screw augmentation. Zhang et al. (2006) also presented a rectangular-shaped bone FEM (12 x 12 mm) with a cortical shell (Zhang et al., 2006). Their model was validated by comparison with an experimental study to measure pullout strength. Their conclusion is that the bone material properties determine the quality of fixation for screw pullout performance.

Abbeele et al. (2017) presented a morphorealistic vertebral FEM to predict intraoperative pedicle screw pullout strength (Abbeele et al., 2017). The model geometry was obtained from micro-CT scans of 30 vertebral specimens and only the pedicle area where the screw is inserted was meshed. The screw had a diameter of 6.1 mm and was modeled as a helical assembly of hexahedral elements. The pullout simulation was validated with their own experimental tests. This was one of the first subject-specific vertebral FEM reported. Their results showed a positive correlation between BMD and pullout strength and stiffness. The experimental results also correlate with the numerical results. As expected, there is a high variability in the results due to the variability found in human vertebrae. From this work, it appears that the geometric representation of the spine in finite element modeling should be implemented to address problems in orthopedic surgery.

Xu et al. (2019) presented a study comparing screw-bone contact simulations during a pullout test and physiological spinal loading test (Xu et al., 2019). Their spine FEM consisted of their previously validated lumbar (L1-L5) model from a 47-year-old male. This model included the cortical shell, cartilaginous endplates, facet joints, and spinal ligaments. A 6.5 x 40 mm single-

threaded non-simplified screw and a simplified screw (no threads) were inserted in the lumbar segment of L3-L4 separately and compared with polyurethane foam FEMs with high and low densities ( $0.32 \text{ g/mm}^3$  and  $0.16 \text{ g/mm}^3$ , respectively). Their goal was to report the effect of screw simplification in a validated vertebral FEM. The results showed a reduced screw anchoring and higher von Mises stress in the simplified screw models. A high-density polyurethane foam FEM showed significantly higher pullout strength than a low-density foam, in both the simplified and non-simplified screws. In conclusion, the bone and screws have higher stresses after implantation during surgery and before the screw and bone are bonded.

Bianco et al. (2017) studied in depth the biomechanics of screw and bone interface during pullout and toggle test with a realistic morphometry of the spine (Bianco, R.-J. et al., 2017). They presented a study analyzing various pedicle screw designs in a lumbar (L3) vertebra model with the SM2S model. Screws were tested as single and dual-threaded, with diameter of 6.5 and 8.5 mm, and length of 40 and 50 mm in a straight-forward and anatomical trajectory. Initial stiffness and peak pullout force were measured. The screw diameter had the most effect on pedicle screw anchorage, meaning that a high diameter size results in better fixation. Cylindrical single-lead threaded screws also had a better anchorage compared to conical screws. However, the shape and mechanical properties of this model remain “generic”, and authors suggested the addition of patient-specific geometry and inclusion of anisotropic properties in future studies.

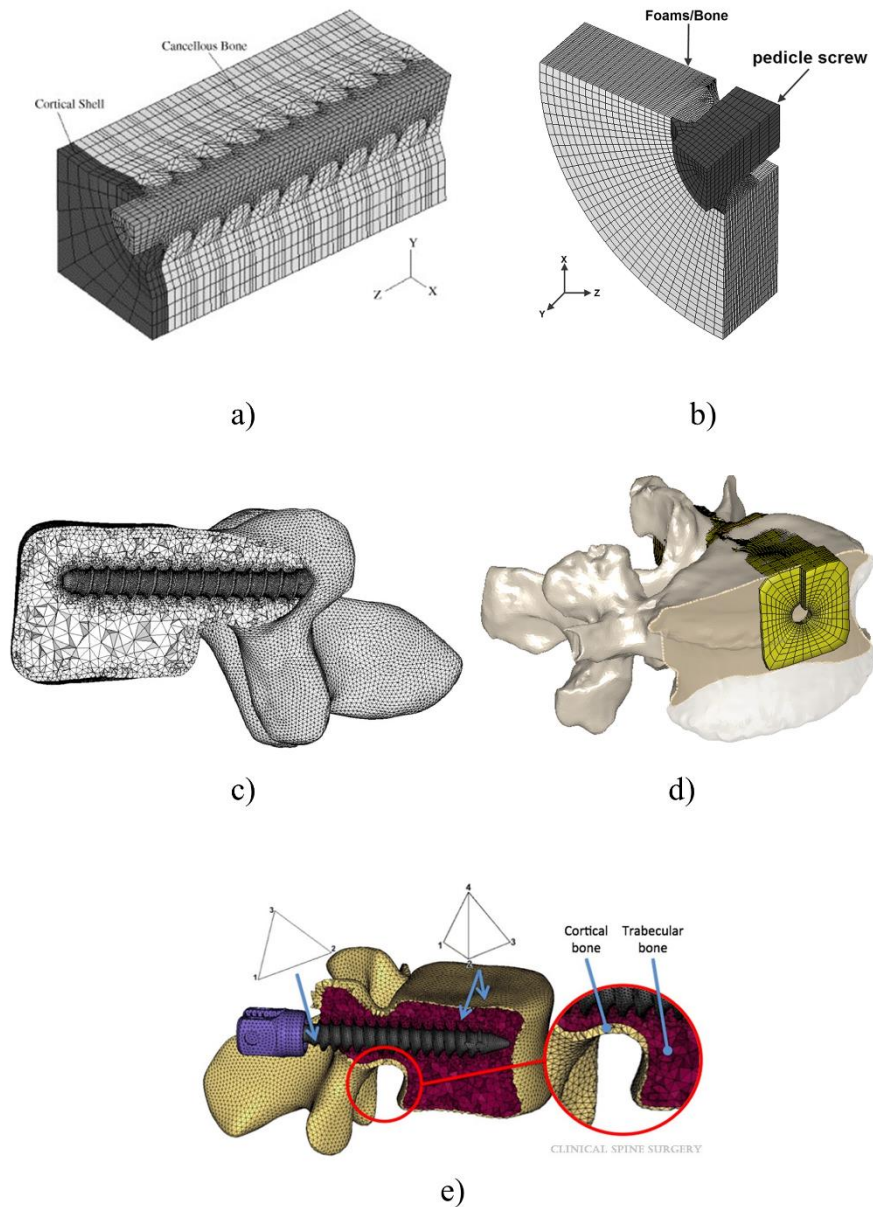


Figure 2.8 Pedicle screw finite element models presented in this section: a) Zhang et al. (2006), b) Liu et al. (2014), c) Xu et al. (2019), d) Abbeele et al. (2017), e) Bianco et al. (2017). Reproduced with permission.

### 2.4.3 FEM refinement using imaging modalities

Different imaging modalities have been used to enhance vertebral FEMs, particularly to account for patient-specific properties. The vBMD, as previously discussed, is widely distributed

throughout the vertebral body and can therefore be defined by advanced imaging modalities such as qCT and micro-CT.

As the CT scanners are calibrated with the X-ray attenuation of water, the resulting measures on the images are called Hounsfield Units (HU), where water is 0 HU. A high HU number represents high density, such as the bone. In qCT, a phantom with known densities is placed below the patient during CT acquisition to transform HU into vBMD ( $\text{g}/\text{cm}^3$ ) (Adams, 2009). To create qCT-based FEM, the voxels from the images are transformed into volumes and then meshed into finite elements. The resulting bone mineral densities are also included in each volume of the qCT-based FEM.

Various qCT-based FEMs have been designed to study vertebral strength and stiffness. Crawford et al. (2003) presented a qCT-based “voxel” FEM and compared it to standard QCT measures for BMD to establish better predictions of vertebral compressive strength (Crawford et al., 2003). Their model consisted of eight-node brick elements with voxel size of  $1 \times 1 \times 1.5 \text{ mm}^3$ . The elastic modulus was estimated from the qCT-derived BMD. Their results showed that a qCT-based FEM is a better predictor than correlation-based (correlation between elastic modulus and QCT-derived BMD) QCT methods to predict vertebral strength and is therefore an important step in the development of new models for clinical applications. Later, Buckley et al. (2007) presented a qCT-based FEM as well using thoracolumbar cadaveric spines to measure vertebral strength (Buckley et al., 2007). Their model was meshed with a 1 mm element size and used isotropic bone mechanical properties. Average trabecular BMD was measured in one region of the vertebral body and compared to integral BMD, where the entire bone volume, including cortical shell and endplates, was considered. The latter accounted for 62% of the variability in experimental testing for vertebral strength, whereas the average density accounted only 16%. Authors concluded that in *in vitro* vertebral experiments, both geometry and the distribution of material properties should be considered.

Unnikrishnan et al. (2013) considered the anisotropic behavior of trabecular bone in their qCT-based FEM (Unnikrishnan et al., 2013). Models designed as a trabecular column and as a morphorealistic vertebral body were assigned generic-anisotropic and specimen-specific properties, obtained by qCT and microCT. Axial stiffness was measured for all models. They concluded that the stiffnesses obtained in the vertebral body qCT-based model, both material

property categories correlated greatly between each other, compared to an uncorrelation for the trabecular column model. As the latter model was only meshed around the center of the vertebral body, the results suggest that including the peripheral regions of the vertebral body in qCT-based models greatly contributes to the mechanical behavior of the bone.

There are several factors that limit the use of CT scanners in clinical applications for patients. To effectively correlate grey values from qCT images in a spine FEM, this process can be time consuming and expensive. Furthermore, the most important limiting factor of CT is the high ionizing radiation, on the order of 8 to 15 mGy for the chest and abdomen acquisitions (Smith-Bindman et al., 2009). Considering that a patient treated for a spinal deformity will undergo routine examinations for follow up, the use of ionizing imaging may be detrimental to his/her health. For example, it has been reported that patients with scoliosis receive up to 177 mGy per year when combining CR and CT with fluoroscopy for their pre- and post-operative follow up (Presciutti et al., 2014). Thus, other imaging modalities with lower radiation emission are to be preferred.

## **2.5 Principles of dual-energy imaging**

Dual-energy X-ray absorptiometry (DXA) is a technology that allows the acquisition of radiographic images and visually separates the underlying tissues. DXA is mostly used in clinic to diagnose different types of bone disease, such as osteoporosis. The principles of DXA are based on the physics of absorptiometry and have been thoughtfully studied not only for diagnostics, but to enhance the comprehension of bone distribution.

During emission, X-rays interact with the tissues in three manners: with Compton scattering, coherent scattering, and photoelectric absorption. The first occurs when the emitted photons lose energy to electrons and scatters in a new direction, reducing image contrast and increasing radiation risk to the environment. Coherent scattering is a less occurring phenomenon (<10%), where the emitting photon binds to the electron's atom and makes it resonate to the incoming photon's frequency. Lastly, the photoelectric absorption effect occurs when the emitted photon ejects an electron from an inner shell from its orbit and becomes absorbed. An electron from an outer shell will take the place of the ejected electron, creating a change of energy between the shells. This in turn creates a characteristic X-ray that has an energy equal to the difference of binding energies between the outer shell electron and the ejected electron, which at the end is quickly absorbed

locally. The probability of this phenomenon happening increases when the energy of the emitted photon (X-ray) is equal or greater than the binding energy of the ejected electron. This is named the “absorption edge” or “K-edge” and it depends on the atomic number ( $Z$ ). In the case of bone, for example, calcium (Ca) has an atomic number of 20 and thus a higher probability of this phenomenon (International Atomic Energy Agency, 2011; Webb, 2003). This absorption process contributes to the overall attenuation of X-rays that pass through a tissue, represented as the Beer-Lambert law:

$$I = I_0 e^{-\mu t} \quad (2.1)$$

where:

$I$ , attenuated X-ray intensity

$I_0$ , unattenuated X-ray intensity

$\mu$ , total linear attenuation coefficient ( $\text{cm}^{-1}$ )

$t$ , tissue thickness (cm)

Linear attenuation coefficients depend on energy and atomic number. Mass attenuation coefficients can also represent attenuation and depend on tissue density. Therefore, for bone and soft tissues, the attenuation coefficients are different depending on the emitting energy (Figure 2.9). Evidently, both tissues could have very similar coefficients given a certain energy. X-ray tube voltages must therefore be modulated in order to only visualise one tissue separated from the other. Additionally, aluminum and polymethyl-methacrylate (PMMA) are two materials that have a similar mass attenuation coefficient to bone and soft tissue, respectively. They are commonly used in phantom design and calibration for DXA imaging.

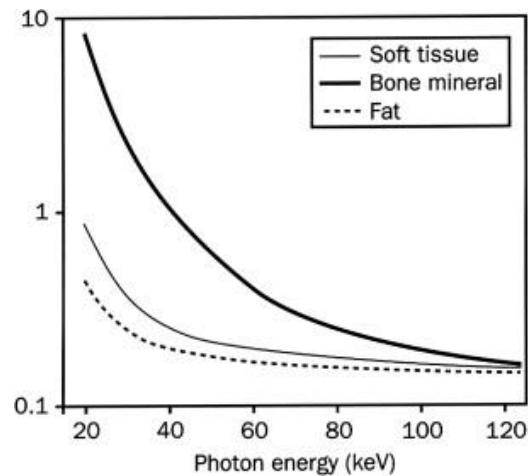


Figure 2.9 Mass attenuation coefficients for bone, soft and fat tissue. From “Skeletal Imaging”, by M.R. Allen and K. Krohn, in D.B. Burr and M.R. Allen (Eds.), *Basic and Applied Bone Biology* (1<sup>st</sup> ed., p.93-113), 2014, Academic Press (<https://doi.org/10.1016/B978-0-12-416015-6.00005-8>). Copyright 2014 by Elsevier. Reproduced with permission.

In clinical DXA, two radiographs can be taken to modulate the energy for bone and soft tissues, so clear images of only bone are used for diagnostics. With the advance of technology, DXA is used to evaluate bone density and quantify it for other applications such as biomechanics.

In the literature, DXA has been used as a tool create detailed bone FEM. Since DXA is a common tool to study the diagnosis of osteoporosis, examinations are commonly done on the patient’s hip. Therefore, most of the studies for 3D-based shapes or FEMs with DXA are done on the proximal femur.

Whitmarsh et al. (2011) presented a method for 3D reconstruction of the shape and BMD distribution of the proximal femur using one single DXA image (Whitmarsh et al., 2011). A statistical model of the combined shape and distribution was used. The 3D reconstruction was built from intensity-based 3D-2D registration process, which allows an instance of the model to maximize the similarity between the projection and the DXA image. Their accuracy error was 1.1 mm between reconstructions and qCT scans. Their aim was to present this method to improve diagnosis of osteoporosis and evaluate fracture risk assessment in future research.

Väänänen et al. (2015) presented a method for 3D reconstruction of the proximal femur with the aim to improve prediction accuracy for hip fracture (Väänänen et al., 2015). Three image sets of

cadaveric and patient CT scans and DXA were used to form two statistical appearance models (SAMs) from 2 image sets. A 3D shape of the femur was reconstructed with DXA and was aligned with the SAM. FEMs were built from the 3D shapes with a good mesh quality. Their limitation however is that their method was not fully automated and depended on a single 2D DXA image. Therefore, the SAM had some errors in shape reconstruction. DXA-based FEMs explained 85% of CT predicted strength of the femur in stance loading. Their mean point-to-surface error was 1-1.4 mm.

Humbert et al. (2017) continued the work of Whitmarsh et al. (2011) with the same methods to 3D reconstruct the proximal femur with separate assessment of the cortical thickness and trabecular bone (Humbert, Ludovic et al., 2017). Their method presented a fully automated algorithm that reduced computing time (1 min 30 s, compared to 1 hour from Whitmarsh et al. (2011), and 40 hours from Väänänen et al. (2015)) and average point-to-surface distance (0.93 mm, compared to 1.1 mm from Whitmarsh et al. (2011) and 1.42 mm from Väänänen et al. (2015)).

Few other studies have presented methods to build spine FEM from DXA images. Since the spine is best represented in a 3D perspective, bi-planar radiology has been used to assess the issue of using one DXA image. EOS Imaging© has designed in the past decade multiple versions of bi-planar radiography technology using simultaneous acquisition of standing patients using two detectors. Conventional low-dose radiographs are ultimately obtained in order to be used in stereoradiography algorithms and reconstruct the spine in 3D (Dubousset et al., 2005). Humbert et al. (2009) presented a method to automatically reconstruct the spine of 175 subjects using bi-planar radiography from EOS and conventional radiography (Humbert, L. et al., 2009). Their novel method consisted of parametric models based on longitudinal and transversal inferences. Two levels of reconstructions were made, with computational time of 2 min 30 s and 10 min, respectively. The mean shape accuracy was 1.3 and 1 mm when compared to CT scan, respectively for both levels of reconstruction. Authors suggested their reconstruction method could be for routine clinical use as an alternative to other methods.

In his thesis, Le Bras, (2004) also used the EOS technology to create multi-energy acquisition protocols (Le Bras, 2004). Four different X-ray voltages and currents were set using different metallic filters to suppress low energy photons during acquisition on cadaveric femurs. Using the absorptiometry theory, BMD was calculated and compared to DXA bone density values. A high

correlation was found between the use of both technologies, although BMD from EOS was overestimated. A high correlation was also found when modifying the acquisition protocol to two energies (dual-energy). The results of both protocols suggest the feasibility of dual- and multi-energy capability with low-dose radiography to estimate accurate BMD, in this case, of the femur.

Later, Choise et al. (2018) presented a methodology using a similar principle as Le Bras but for the spine. EOS technology was used to acquire radiographic images of cadaveric lumbar spines (L1-L3) by modifying the energy twice, creating high and low dose images and allowing an estimation of vBMD. A FEM created from bi-planar radiography was generated, and results suggested it was comparable to a qCT-based spinal FEM in the prediction of vertebral strength.

Lastly, Sapin de Broses et al. (2010) presented a methodology to predict the mechanical properties of the trabecular bone using EOS bi-planar radiography (Sapin de Broses et al., 2010). Nineteen thoracic samples (T10-T12) were imaged with low and high energy, along a previously established protocol to assess a dual-energy modality (Sapin et al., 2008). Density values were measured from PA and LAT radiographs and correlated with experimental measurements from the same vertebral samples. Young's modulus was predicted using areal bone mineral density and correlated with QCT-based density-mechanical properties regressions. Their study demonstrated the feasibility of using EOS bi-planar radiography technology to estimate bone density and mentioned their future feasibility for FEM.

Bi-planar technology has been shown to be an effective solution to build spine FEMs using low-dose imaging. However, there are no studies that evaluate the performance of orthopedic instrumentation in spine FEMs using bi-planar radiography. Additionally, the advantages of dual-energy (DE) to estimate vBMD could enhance vertebral FEMs with accurate representation of bone distribution.

### **2.5.1 Description of a novel imaging system with dual-energy radiography**

To pursue the advantages of DE radiography, a novel low-dose DE imaging system was acquired for this study. Due to a confidential agreement, the name of the company is omitted throughout this document. It has the capacity of generating simultaneous bi-planar radiographs in a frontal and lateral view of a patient in a standing, physiological weight-bearing position. Two X-ray tubes are

placed in front of their respective photon-counting detectors and simultaneously acquire upright high-resolution images. This system uses a technology of dual-energy absorptiometry to change between a low and high X-ray energy into the tissues, allowing the calibration of the radiographic images with the appropriate material with similar absorption coefficients, that is, PMMA and aluminum for soft and bone tissue respectively. Moreover, images are also calibrated in the density of hydroxyapatite (HA), which allows a pixel-level representation of bone density calibrated images. The resulted images are given in a DICOM format for post-processing.

Additionally, to generate radiographic images in a controlled environment, the company provided an image simulator. This allows the generation of simulated DE radiographic images using a patient's CT-scan previously acquired. The acquisition parameters can be set in this simulator as if taken directly on the imaging system. The resulted images are the same as the ones obtained by the system. The simulator allows a freedom of radiographic image acquisition for a more controlled experimental process. A detailed description of the system is mentioned in Chapter 4.

## **CHAPTER 3      RESEARCH OBJECTIVES AND ORGANIZATION OF THE WORK**

The literature review presented in the previous chapter has allowed an identification of main points that will structure this project's objective:

- Bone tissue presents anisotropic properties, which vary according to loading directions and anatomical region, creating a heterogeneous distribution of bone mineral density throughout the vertebral body and posterior elements.
- The anterior and central regions of the vertebral body have lower bone mineral density, whereas the posterior regions have a higher density.
- There is a mathematical relationship between bone rigidity and mineral density thoroughly studied in the literature, which is highly variable from the sources.
- Thus, there is a high variability on the measured mechanical properties of the bone due to the variability of human bones (age, weight, condition, vertebral region, methodology, etc.)
- Bone quality is a factor that affects pedicle screw fixation, as it has been shown in experimental literature on pullout testing.
- Finite element modeling of the spine allows a detailed biomechanical analysis for orthopedic instrumentation.
- Generic mechanical properties and bone quality homogeneous representation is used in spine FEM, which limits the inclusion of subject-specific properties.
- Dual-energy has been shown to be equality feasible as an alternative solution for spine FEM refinement compared to CT technology, which is limited by its high cost and high ionizing radiation exposure.

Using the novel DE imaging modality described in Chapter 2.5.1., this is a first-time project to evaluate the capability of this technology in a vertebral finite element model for the evaluation of orthopedic instrumentation.

### **3.1 Objectives**

The overall objective of this master's research project is to develop and evaluate the feasibility of integrating patient-specific mechanical properties of the bone using dual-energy radiography in a 3D vertebral finite element model to improve pedicle screw fixation modeling.

#### **3.1.1 Specific objectives**

In order to achieve the general objective of this master's project, three specific objectives were defined:

1. Create a protocol for dual-energy radiographic image acquisition specific to spine analysis.
2. Design a functional methodology to relate calibrated radiographic images for bone, obtained with the novel dual-energy radiographic system, to the mechanical properties of the vertebrae.
3. Evaluate the performance of pedicle screw fixation in a vertebral finite element model that includes the mechanical properties derived from dual-energy radiographic images.

### **3.2 Organization of the work**

This article-based thesis is organized into seven chapters described as follows:

- Chapter 1 presented the introduction of the project.
- Chapter 2 presents the review of knowledge of this project.
- Chapter 3 presents the objectives of the project and organization of the thesis.
- Chapter 4 presents a scientific article that describes the methodology to estimate vertebral mechanical properties and the results of pedicle screw pullout simulation in a vertebral finite element model.
- Chapter 5 presents a framework for the vertebral finite element model, describing the methodology to identify the best parameters to use in the pedicle screw pullout simulation.
- Chapter 6 presents the discussion of this project.

- Chapter 7 presents the conclusion and recommendations for future work.
- Appendices 1 and 2 briefly present the methodology to estimate volumetric bone mineral density for two types of isotropic vertebral finite element models with different bone distributions.

### 3.3 Methodology overview

The methodology followed in this study is described in Figure 3.1. First, the DE radiographs are generated from a CT-scan test-case using the company-provided DE image simulator. A selection of regions of interest within the HA-calibrated images is done to estimate the vBMD. Then, using an equation that relates vBMD and bone rigidity is used to estimate the Young's modulus. Additional mechanical properties of the bone are thoughtfully selected from the literature. Finally, a pedicle screw pullout simulation is done on the vertebral FEM where different parameters are measured to evaluate screw fixation.

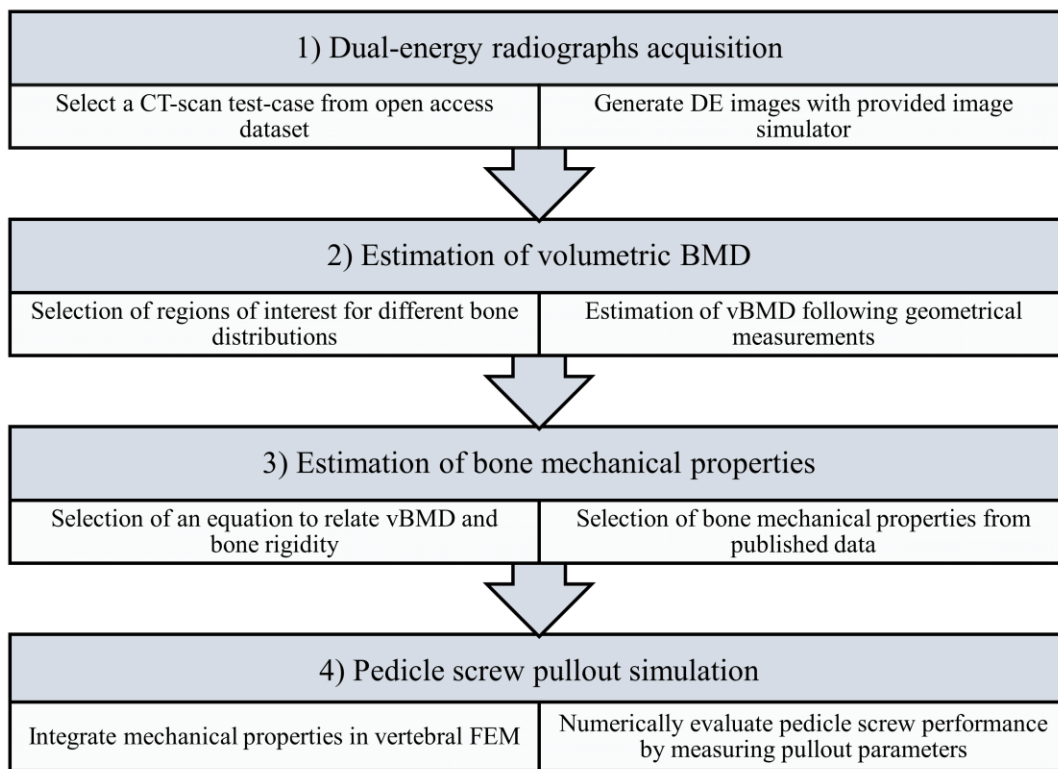


Figure 3.1 Methodology overview for the present study.

## **CHAPTER 4      ARTICLE 1: TOWARDS A PATIENT-SPECIFIC VERTEBRAL FINITE ELEMENT MODEL USING DUAL-ENERGY RADIOGRAPHY IMAGING TO IMPROVE PEDICLE SCREW FIXATION**

### **4.1 Presentation of the article**

The research article presented in this Chapter describes the methodology followed to estimate the mechanical properties of L3 on a case-test using dual-energy radiography and integrating them into a vertebral FEM. This article addresses the specific objectives mentioned in Chapter 3. The article entitled “Towards a patient-specific vertebral finite element model using dual-energy radiography imaging to improve pedicle screw fixation” was submitted to the “Journal of Medical & Biological Engineering & Computing” on January 13<sup>th</sup>, 2022. The first author contributed to 85% of the preparation and writing of this article.

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## 4.2 Abstract

Instrumentation and fusion are used to treat severe spine deformities. Failure of pedicle screw fixation is a problem primarily related to the mechanical properties of the bone. The objective was to develop and validate a vertebral finite element model (FEM) that includes patient-specific mechanical properties of the vertebrae derived from a new low-dose dual-energy (DE) radiography system. Hydroxyapatite density-calibrated radiographs were used to estimate the volumetric bone mineral density of the vertebrae and the mechanical properties were derived using published mathematical equations. Two isotropic FEMs of L3 were defined with averaged (homogeneous) and averaged over small regions of interest (heterogeneous) trabecular bone distribution. Pedicle screw axial pullout was simulated and the distribution of maximum stresses, peak pullout force and bone-screw interface stiffness were calculated and compared between the models. Subject-specific bone characteristics derived from DE radiographs influenced the performance of simulated pedicle screw extraction. Bone-screw interface stiffness, maximum pullout force, and the stress distribution magnitudes were higher for models with mechanical properties derived from DE images. Consideration of individualized bone distribution in a spinal FEM allows a more realistic perspective for orthopedic surgical planning compared to otherwise underestimated results using a homogeneous reference distribution.

**Keywords:** Finite Element Modeling, Dual-Energy Radiography, Patient-Specific Modeling, Pedicle Screw

## 4.3 Introduction

Spine deformities affect 1.4 to 32% of adults over the age of 60 [41]. In 34% of cases, a surgical intervention is needed to straighten and fuse the spine using instrumentation, consisting of contoured rods connected to pedicle screws [3].

Pedicle screws need a proper purchase to sustain the loads exerted to correct the deformity and maintain it during the time needed to fuse the spine. For a given screw diameter and length, the fixation strength depends on the quality of the trabecular bone [37, 38] and the thickness of the cortical bone traversed by the screw trajectory. The risk of pedicle screw failure has been reported in 0.8 to 27% of the cases [10, 19], with screw dimension and trajectory being important

determinants [8]. Additionally, poor bone quality (as found with osteoporosis) contributes to poor anchoring and thus screw fixation planning should be separately considered from healthy vertebrae [24, 38].

To evaluate pedicle screw performance, standard pullout tests are often used experimentally on cadaveric or foam specimens [26, 35, 37], which limits the very diverse representation of vertebral characteristics in the adult spine deformity population. As an alternative, finite element modeling (FEM) can provide detailed biomechanical analysis and numerically simulate pullout tests to evaluate the performance of the screw/vertebra interaction. Spine FEMs have been used to predict vertebral fracture [15, 43] or pedicle screw failure [12], but also, to assess screw fixation performance or vertebral fusion [8, 16]. Spine models are usually designed with a generic geometry and average mechanical properties [17, 36]. Patient-specific spine models have been developed [1, 39], both in terms of geometry and mechanical properties, which intended to provide a more realistic representation of the instrumentation simulation [39].

Geometric and material properties of bone tissue can be obtained via imaging modalities such as computer tomography (CT). Other modalities include quantitative computer tomography (qCT), where the grey values on the images are correlated with known phantom densities to estimate the volumetric bone density of human vertebrae [4, 34], and micro-CT, where the properties of single bone human specimen can be analyzed at the sub-tissue level [13, 14, 18]. A great variation and heterogeneity of the mechanical properties of the vertebral body has been reported, especially between peripheral and central regions [5, 6, 18, 32, 34]. Anisotropy attributable to Wolff's law is also reported for trabecular bone [30]. CT or qCT requires correlating density and stiffness values with measured gray levels, a relatively long, complex, and expensive process in clinical practice. Also, these imaging techniques impose high levels of ionizing radiation on the patient [40], which limits their use.

We recently acquired an off-label version of a low-dose multi-energy imaging system with the capacity of acquiring simultaneously bi-planar (lateral and frontal) radiographs of a patient in a standing, physiological weight-bearing position. Two X-ray fan beam tubes are used along with respective photon-counting detectors to simultaneously acquire upright high-resolution images. This system uses a technology of dual-energy (DE) absorptiometry to modulate a low and high X-ray energy into the tissues. Following the Beer-Lambert's law, bone and soft tissue can be visually

separated according to their absorptiometry coefficients, which are energy dependent. Additionally, with the proper calibration of bone-targeted images, they provide high-resolution information of the geometry and bone mineral density of the vertebrae and pelvis.

The purpose of this study was to develop and evaluate the feasibility of integrating patient-specific mechanical properties of the bone tissue using DE radiography in a 3D vertebral FEM, in order to improve pedicle screw fixation modeling.

## 4.4 Methods

### 4.4.1 Dual-energy radiographic images

In this feasibility study, we used synthetic radiographic images generated using a company-provided simulator to simulate controlled posteroanterior (PA) and lateral (LAT) radiographs in DICOM format (Figure 4.1), exactly like those generated by the DE imaging system. The simulated acquisition parameters were 130 kV and 125 mA for X-ray tube voltage and current, respectively, with a 0.1 mm copper filter. Pixel size of the images was set at 0.1 mm.

A test case was derived from an open access CT scan from the dataset acquired by the Department of Radiology at the University of Washington and published online by the Department of Computing at Imperial College London (BioMedIA) [22, 23], enabling to generate DE radiographs only of the spine. Four simulated radiographs were generated for each view: a contour-enhanced image, a polymethyl methacrylate (PMMA) calibrated image, an aluminum (AL) calibrated image, and a hydroxyapatite (HA) density calibrated image which simulates the bone mineral density of the acquired bone structures. Hydroxyapatite is a mineral found in calcium apatite which has similar properties to human bone mineral. The PMMA and aluminum calibrated images simulate respectively soft and bone tissue due to their similar absorptiometry coefficient. For both PMMA and aluminum calibrated images, the DICOM scale attribute is “mm of PMMA” and “mm of AL” respectively. For the hydroxyapatite calibrated images, this scale is “g/cm<sup>2</sup>” as the images are calibrated with the density of this mineral. The pixel intensity value for HA-calibrated radiographs is therefore shown in the unit of bone mineral density (g/cm<sup>2</sup>).

#### **4.4.2 Definition of the vertebral models**

From the simulated DE radiographs, the HA-calibrated images were used in this study to estimate the mechanical properties of the test case (referred thereafter as patient-specific mechanical properties). A reference FEM was built, for comparison purposes, using published mechanical properties (referred thereafter as reference mechanical properties). For this feasibility study, the methodology was tested for the 3rd lumbar vertebra (L3).

Four isotropic FEMs of L3 were created with two different trabecular bone distributions derived from the DE radiographs or from published trabecular bone mineral density with mechanical properties estimated using published mathematical equations [31]: 1) averaged (homogeneous) and 2) averaged over small regions of interest (heterogeneous), as shown in Figure 4.2.

For the heterogeneous models, eight different subregions (A-H) were defined to differentiate the mechanical properties of the anterior and posterior parts of the vertebral body as well as the superior and inferior regions (Figure 4.2b), following the work of Zhao et al. [46] and Wagnac et al. [43]. The posterior elements were also separated from the vertebral body, with two subregions in the pedicles.

#### **4.4.3 Estimation of volumetric bone mineral density**

##### **4.4.3.1 Estimation of volumetric bone mineral density from dual-energy HA-calibrated radiographs**

The pixel intensity values of the HA-calibrated radiographs obtained from the image simulator were defined as surface bone mineral density ( $\text{g}/\text{cm}^2$ ). The volumetric bone mineral density was computed in the trabecular region for the homogeneous model and the 8 regions of interest (ROI) for the heterogeneous model for each radiograph using ImageJ (ImageJ 1.53a, National Institutes of Health, USA, Maryland). The surface area and the average pixel intensity value within each ROI was computed using a measuring tool in ImageJ. Average pixel intensity was converted as HA mineral density ( $\text{g}/\text{cm}^2$ ) using the corresponding DICOM attributes.

From the surface area and calculated density, the analytic approach from Carter et al. [11] was followed to estimate the volumetric bone mineral density ( $\text{g}/\text{cm}^3$ ), adding a 3D perspective into the

estimation. Bone mineral content (BMC) was computed as  $BMC = A * BMD$ , where  $A$  is the surface area and BMD is the bone mineral density (or average pixel intensity value) from the selected ROI. Next, the depth of the ROI was estimated to assess a 3D perspective of the ROI's shape. To simplify the process, the volumetric shape of the trabecular bone on the vertebral body ROI was assumed as a rectangular prism. From the LAT image, the length of the vertebral body was measured to estimate the PA view depth, and conversely for the PA image. For the pedicle region, the shape was assumed as a cylindrical prism. Afterwards, the volume was estimated as  $Volume = depth * A$ . Finally, the volumetric bone mineral density was estimated as  $vBMD = BMC / volume$ .

This process was followed on both PA and LAT radiographic images for the homogeneous (Table 4.1) and for the heterogeneous (Table 4.2) models. The posterior elements' parameters were estimated using the trabecular superior-posterior subregion since their densities are similar.

#### 4.4.3.2 Estimation of reference volumetric bone mineral density from published data

The volumetric bone density for the reference model (homogeneous and heterogeneous) was estimated from the reported work of Banse et al. [6] (Table 4.3). Based on the reported 48 samples of 8 lumbar vertebrae, the average density values were applied to the entire trabecular bone of the vertebra. As for the heterogeneous model, an analogous approach of average by subregion was used. The average of all obtained volumetric bone mineral densities was used as the single value of volumetric bone mineral density for the homogeneous model.

#### 4.4.4 Computation of the mechanical properties

The mechanical properties of cortical and trabecular bones were represented by an elastoplastic material law (Johnson-Cook) [20]. The Young's modulus (MPa) was defined from the vBMD according to the equation published by Keller et al. [31] (Equation 4.1). Other mechanical properties, such as the Poisson's ratio, the yield stress (MPa) the hardening modulus (MPa), the hardening exponent, the failure plastic strain, and the plasticity maximum stress (MPa), were obtained from previous studies that used an inverse finite element method from experimental tests [20, 21, 43].

$$E = 1.89 vBMD^{1.92} \quad (4.1)$$

Equation 4.1 was used to estimate the Young's modulus for the homogenous and heterogeneous models, from the trabecular vBMD of DE radiographs (Tables 4.1 and 4.2) and the trabecular vBMD estimated from published data (Table 4.3). Cortical bone's mechanical properties were defined from the published literature. The mechanical properties computed from published data and derived from DE radiographs are shown in Tables 4.3 and 4.4, respectively, and in Figure 4.3.

#### **4.4.5 Vertebral finite element model**

The baseline FEM geometry of L3 was first extracted from the SM2S (Spine Model for Safety and Surgery) model corresponding to a CT-scan of a 32-year-old male volunteer in the 50th percentile [17]. It includes its vertebral body, the pedicles, and posterior elements. The cortical bone had a thickness varying between 1.0 to 1.5 mm. The trabecular and cortical bone were meshed with 4 node tetrahedral elements whose characteristic size was 0.5 mm to 1 mm in the vicinity of the screws [7-9]. The FEM was generated using Hyperworks v2014 (Altair Engineering Inc., 2014, USA, Michigan).

The homogeneous models had only the trabecular and cortical bone volumes. The heterogeneous models were modified so the trabecular bone boundaries were separated into the 8 subregions defined in section 4.4.2. Figure 4.4 shows the resulting four vertebral FEMs.

##### **4.4.5.1 Pedicle screw pullout simulation**

The pedicle screw used in this model was a cylindrical equally spaced single-lead thread screw (CD Horizon Legacy screw). The screw was modeled as a rigid body with 0.5 mm shell triangular elements. The screw had a 6.5 mm diameter and a 40 mm length and was inserted in the model on the right pedicle in a straight-forward trajectory (Figure 4.4). A penalty-based contact was used on the bone-screw interface with a Coulomb-type friction coefficient of 0.2 and a minimal gap of 0.03 mm [8]. A displacement rate of 0.1 mm/ms was simulated to create an axial load until the peak force was reached. Boundary conditions were applied in the external nodes of the anterior portion of the vertebral body and in the screw head [8]. The latter was established with a constraining slide link condition so the screw would slide out without an off-axis displacement during the simulation. The solver used for these quasi-static simulations was RADIOSS v2013 (Altair Engineering Inc., 2013, USA, Michigan).

From the pullout simulations, three dependent parameters were post-processed to evaluate the performance of the pedicle screw fixation: the peak pullout force (MPa), the bone-screw interface initial stiffness (N/mm) and the distribution of maximum stress in the bone around the screw (MPa). The peak-pullout force was reported as the maximum pullout force recorded in the force-displacement curve. The initial stiffness was calculated for the most linear initial part of the slope of force-displacement curve. Finally, the maximum stress distribution was calculated as the Von Misses stress distribution using the HyperView v2013 tool (Altair Engineering Inc., 2013, USA, Michigan)

## 4.5 Results

The maximum stress distribution was concentrated in the bone at the screw threads all along the entire length of the screw and was essentially the same for all four models tested (Figure 4.5). The maximum stress was rather similar between 2.57 MPa and 2.66 MPa for all four models.

However, the force-displacement curves and initial stiffness were quite different between the four models (Figures 4.6 and 4.7). The initial stiffnesses for the models from DE images were 5262 N/mm and 4830 N/mm for the homogeneous and heterogenous representations of the trabecular bone, respectively, while for the reference models it was 2232 N/mm and 2314 N/mm. Therefore, the stiffness of the models from the DE images was 58% and 52% higher than the homogeneous and heterogeneous reference models, respectively. The peak pullout forces for the models from DE images reached 418 N and 511 N for the homogeneous and heterogeneous models, respectively, while for the reference models, they were 28% lower (297.8 N and 371 N) (Figure 4.7).

The models from DE images reached a peak pullout force at a smaller simulated screw displacement than the reference models (0.1 mm vs. 0.15 mm, respectively) for the homogeneous models. The same tendency was seen for the heterogeneous models (0.14 mm vs. 0.2 mm).

## 4.6 Discussion

The novel DE imaging technology allowed to characterize the case-specific mechanical properties, which had a clear impact on the simulation of screw pullout vs. using published reference properties as done in most reported studies [1, 8, 45]. These differences are mostly seen in the peak pullout

force during pullout simulation and the initial stiffness of the bone-screw interface. This can be explained by the fact that the vBMD values ( $\text{g/cm}^3$ ) of the DE images were slightly higher than those of the reference models (Tables 4.1 and 4.2), especially in the pedicle region where the vBMD is 3 times higher than in the posterior regions. Consequently, the posterior elements, the pedicles and the posterior regions of the vertebral body of the heterogeneous models had higher Young's modulus compared to the homogeneous models, which also contributed to higher pullout force and stiffness. These differential properties cause the posterior subregions to provide better resistance at the first quarter of the pedicle screw length during simulated pullout, as shown in the work of Hirano et al. [25] that the pedicle region contributes 80% of the bone-screw stiffness and 60% of the pullout strength.

A strength of the DE imaging system used in this study is to provide calibrated HA radiographs, which allows a detailed quantification of the mechanical properties of vertebral bone to incorporate a more realistic distribution of bone tissue in the vertebral FEMs. Published studies have presented a similar work on estimating a heterogeneous representation of BMD distribution with single-image dual-energy X-ray absorptiometry (DXA) [28, 42, 44] and bi-planar radiography [15, 27], but have not focused on quantifying mechanical properties for orthopedic instrumentation fixation.

The observed relationship between bone density and resulting peak pullout force is consistent with the work reported by Liu et al. [37]. Furthermore, the simulated screw pullout forces in the current study are similar to the reported values which ranged from 221 N to 702 N for a Young's modulus variation from 60 MPa to 220 MPa. The overall maximum stresses for all models in the current study, ranging from 2 to 2.6 MPa, are similar to slightly higher than the stresses around the pedicle screw area reported by Liu et al., which ranged from 0.6 to 2.2 MPa [37]. The initial stiffness of the current study is also comparable to or slightly higher than the values reported from experimental [2, 29] and numerical [8] pedicle screw pullout tests. These differences must be put into perspective considering the difference between the studies, including the fact that these reported tests were performed on animal lumbar vertebrae (calves and mini-pigs), which are different in geometry and mechanical properties from those of human vertebrae, and that the experimental publications did not report bone mineral density values.

The limitations of this study include 1) the need of manual identification of trabecular bone subregions to estimate the vBMD of vertebrae and therefore, the mechanical properties; 2) the

absence of population data of DE radiographic images and therefore statistical analysis; 3) the study was done only on one case, which did not allow to study the effects of inter-individual variability, and 4) a segmentation limited for the moment to 8 subregions. An automatic algorithm would allow rapid calculation of volumetric bone density from bi-planar radiographs, especially since they can be matched via stereography methods. For the heterogeneous model, the manual definition of subregions must be done beforehand; this can be a tedious definition knowing that each subregion can vary from one patient to another. Having an automatic method to estimate the mechanical properties of a vertebra, and even more so, of a section or the entire spine, would allow faster acquisition of these properties for multiple radiographies.

## **4.7 Conclusions**

This study demonstrated the feasibility of spinal FEM with patient-specific mechanical properties by exploiting the potential of bi-planar DE radiography. An increase in bone-screw interface stiffness, peak pullout force and stress distribution around the screw were observed in the models derived from DE images compared to the reference models. For the heterogeneous model from DE images, the initial stiffness and maximum stress distribution was lower than that of the homogeneous model from DE images. A posterior distribution of higher mechanical properties provides better fixation for the pedicle screw.

The ability to better describe the heterogeneity of bone density distribution in a vertebral FEM provides a relevant perspective to improve the quality of FEMs for orthopedic surgery planning.

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## **4.9 Conflict of interests**

Dr. Aubin reports grants from the Natural Sciences and Engineering Research Council of Canada (Industrial Research Chair Program with Medtronic of Canada), and outside of the current work,

contracts with Medtronic. Dr. Villemure has no declaration of interest. Ms. Solorzano-Barrera has no declaration of interest.

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## 4.11 Tables

Table 4.1 Estimated parameters from bi-planar dual-energy radiographs for the homogeneous model for a) the trabecular bone, and b) the cortical bone. The estimated volumetric bone mineral density is shown in bold

| Parameters                                           | Lateral view | Posteroanterior view | Both views   |
|------------------------------------------------------|--------------|----------------------|--------------|
| a) Trabecular bone                                   |              |                      |              |
| Area (cm <sup>2</sup> )                              | 12.636       | 15.907               | -            |
| Average pixel intensity (g/cm <sup>2</sup> )         | 1.040        | 1.329                | -            |
| Bone mineral content (g)                             | 13.141       | 21.141               | 17.141       |
| Depth (cm)                                           | 4.372        | 3.716                | -            |
| Volume (cm <sup>3</sup> )                            | 55.248       | 59.105               | 57.176       |
| Volumetric bone mineral density (g/cm <sup>3</sup> ) | 0.238        | 0.358                | <b>0.298</b> |
| b) Cortical bone                                     |              |                      |              |
| Area (cm <sup>2</sup> )                              | 5.902        | 4.729                | -            |
| Average pixel intensity (g/cm <sup>2</sup> )         | 1.157        | 1.474                | -            |
| Bone mineral content (g)                             | 6.828        | 6.971                | 6.899        |
| Depth (cortical thickness) (cm)                      | 0.289        | 0.738                | -            |
| Volume (cm <sup>3</sup> )                            | 1.706        | 3.490                | 2.598        |
| Volumetric bone mineral density (g/cm <sup>3</sup> ) | 4.003        | 1.997                | <b>3.000</b> |

Table 4.2 Computed parameters from bi-planar dual-energy radiographs for the heterogeneous vertebral model. The estimated volumetric bone mineral density is shown in bold as average vBMD (average from the lateral and posteroanterior view)

| Parameters                                                   | Lateral view |             |             |             |             |             |             |             | Posteroanterior view |          |               |              |               |
|--------------------------------------------------------------|--------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|----------------------|----------|---------------|--------------|---------------|
| Subregions of trabecular bone                                | A            | B           | C           | D           | E           | F           | G           | H           | Superior             | Inferior | Right pedicle | Left pedicle | Both pedicles |
| Area (cm <sup>2</sup> )                                      | 2.23         | 1.93        | 2.01        | 2.40        | 2.01        | 2.07        | -           | 0.95        | 8.46                 | 7.37     | 0.66          | 0.68         | -             |
| Average pixel intensity (g/cm <sup>2</sup> )                 | 0.66         | 0.92        | 1.17        | 0.54        | 1.20        | 1.49        | -           | 1.04        | 1.29                 | 1.35     | 0.93          | 1.21         | -             |
| Bone mineral content (g)                                     | 1.46         | 1.77        | 2.36        | 1.29        | 2.41        | 3.08        | -           | 0.98        | 10.89                | 9.96     | 0.62          | 0.48         | 0.69          |
| Depth (cm)                                                   | 4.37         | 4.37        | 4.37        | 4.37        | 4.37        | 4.37        | -           | -           | 1.24                 | 1.24     | -             | -            | -             |
| Volume (cm <sup>3</sup> )                                    | 9.73         | 8.45        | 8.78        | 10.50       | 8.80        | 9.03        | -           | 0.77        | 10.48                | 9.12     | 0.76          | 0.78         | 0.77          |
| Volumetric bone mineral density (g/cm <sup>3</sup> )         | 0.15         | 0.21        | 0.27        | 0.12        | 0.27        | 0.34        | -           | 1.28        | 0.37                 | 0.29     | 0.82          | 0.61         | 0.90          |
| Average volumetric bone mineral density (g/cm <sup>3</sup> ) | <b>0.26</b>  | <b>0.29</b> | <b>0.32</b> | <b>0.20</b> | <b>0.28</b> | <b>0.31</b> | <b>0.32</b> | <b>0.90</b> |                      |          |               |              |               |

Table 4.3 Mechanical properties computed from published data for the homogeneous and heterogeneous L3 vertebral reference model. Young's modulus was estimated using Equation 4.1. The remaining mechanical properties were obtained from previous published data

| Homogeneous model                       |                 |               | Heterogeneous model          |       |       |       |       |       |       |       | References                          |
|-----------------------------------------|-----------------|---------------|------------------------------|-------|-------|-------|-------|-------|-------|-------|-------------------------------------|
| Mechanical Properties                   | Trabecular bone | Cortical bone | Trabecular bone (subregions) |       |       |       |       |       |       |       |                                     |
|                                         |                 |               | A                            | B     | C     | D     | E     | F     | G     | H     |                                     |
| Volumetric bone mineral density (g/cm³) | 0.169           | 2.0           | 0.16                         | 0.17  | 0.17  | 0.17  | 0.18  | 0.19  | 0.17  | 0.18  | [6, 25] trabecular, [8] cortical    |
| Young's modulus (MPa)                   | 62.23           | 2625          | 52.71                        | 60.82 | 65.09 | 62.94 | 68.01 | 76.36 | 65.23 | 66.54 | [31] trabecular, [8] cortical       |
| Poisson ratio                           | 0.25            | 0.3           | 0.2                          | 0.2   | 0.2   | 0.2   | 0.2   | 0.2   | 0.25  | 0.25  | [8] homogeneous, [43] heterogeneous |
| Yield stress (MPa)                      | 1.95            | 105           | 1.65                         | 1.87  | 1.97  | 1.91  | 2.05  | 2.25  | 1.97  | 1.97  | [8] homogeneous, [33] heterogeneous |
| Hardening modulus (MPa)                 | 16.3            | 875           | 8.5                          | 7     | 8.5   | 8.1   | 12.5  | 12.5  | 7     | 7     |                                     |
| Hardening exponent                      | 1               | 1             | 1                            | 1     | 1     | 1     | 1     | 1     | 1     | 1     | [8] homogeneous, [43] heterogeneous |
| Failure plastic strain                  | 0.04            | 0.04          | 0.082                        | 0.06  | 0.082 | 0.08  | 0.104 | 0.104 | 0.06  | 0.06  |                                     |
| Plasticity maximum stress (MPa)         | 2.6             | 140           | 2.65                         | 2.3   | 2.65  | 2.6   | 3.25  | 3.25  | 2.3   | 2.3   |                                     |

Table 4.4 Mechanical properties computed from dual-energy radiographs for the homogeneous and heterogeneous L3 vertebral model. Young's modulus was estimated using Equation 4.1. The remaining mechanical properties were set from published data ([8, 20, 33, 43])

| Mechanical Properties                                | Homogeneous model |               | Heterogeneous model          |        |        |       |        |        |        |        |
|------------------------------------------------------|-------------------|---------------|------------------------------|--------|--------|-------|--------|--------|--------|--------|
|                                                      | Trabecular bone   | Cortical bone | Trabecular bone (subregions) |        |        |       |        |        |        |        |
|                                                      |                   |               | A                            | B      | C      | D     | E      | F      | G      | H      |
| Volumetric bone mineral density (g/cm <sup>3</sup> ) | 0.298             | 3.0           | 0.26                         | 0.29   | 0.32   | 0.20  | 0.28   | 0.31   | 0.32   | 0.90   |
| Young's modulus (MPa)                                | 184.67            | 2625          | 144.73                       | 177.86 | 213.82 | 90.08 | 164.61 | 204.43 | 213.82 | 213.82 |
| Poisson ratio                                        | 0.25              | 0.3           | 0.2                          | 0.2    | 0.2    | 0.2   | 0.2    | 0.2    | 0.25   | 0.25   |
| Yield stress (MPa)                                   | 1.92              | 105           | 1.65                         | 1.87   | 1.97   | 1.91  | 2.05   | 2.25   | 1.97   | 1.97   |
| Hardening modulus (MPa)                              | 16.3              | 875           | 8.5                          | 7      | 8.5    | 8.1   | 12.5   | 12.5   | 7      | 7      |
| Hardening exponent                                   | 1                 | 1             | 1                            | 1      | 1      | 1     | 1      | 1      | 1      | 1      |
| Failure plastic strain                               | 0.04              | 0.04          | 0.082                        | 0.06   | 0.082  | 0.08  | 0.104  | 0.104  | 0.06   | 0.06   |
| Plasticity maximum stress (MPa)                      | 2.6               | 140           | 2.65                         | 2.3    | 2.65   | 2.6   | 3.25   | 3.25   | 2.3    | 2.3    |

## 4.12 Figures

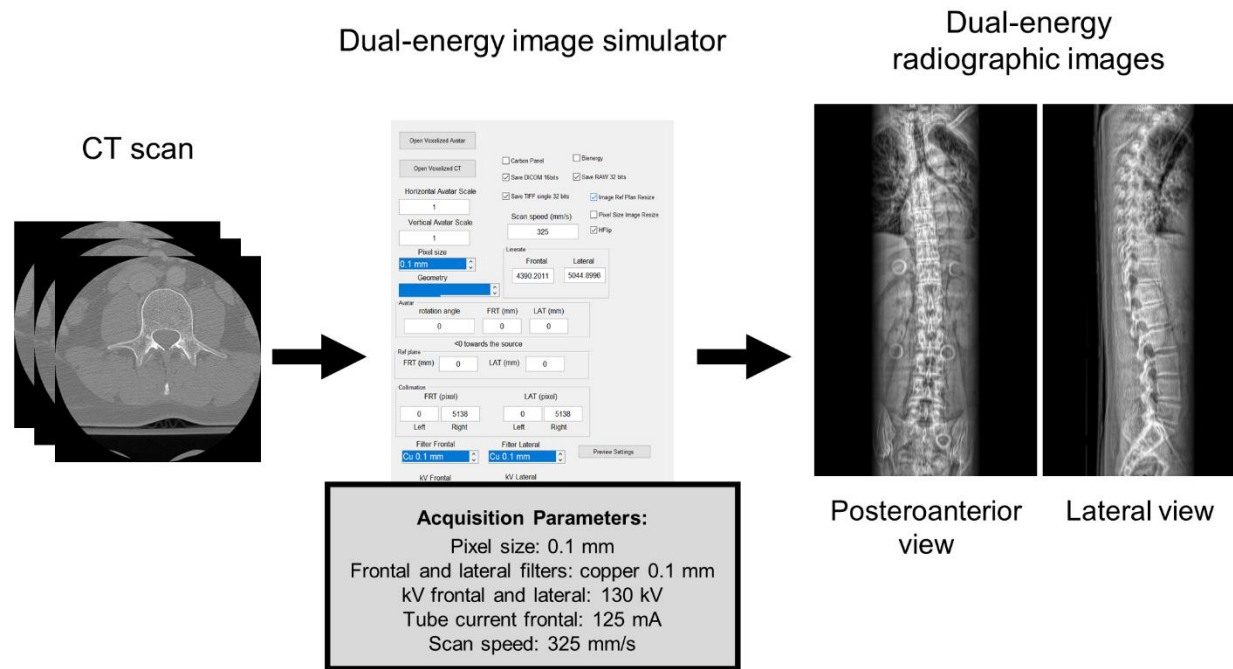


Figure 4.1 For the purpose of the feasibility study, the DE radiographic images were synthetically generated using available CT-scan from BioMedIA [22, 23], using the simulated image acquisition parameters shown above. Four sets of the DE radiographic images were generated to simulate the density of the acquired spine structures: 1) contour-enhanced image, 2) polymethyl methacrylate (PMMA) calibrated image (soft tissue), 3) aluminum (AL) calibrated image (bone tissue), and 4) hydroxyapatite (HA) density calibrated image

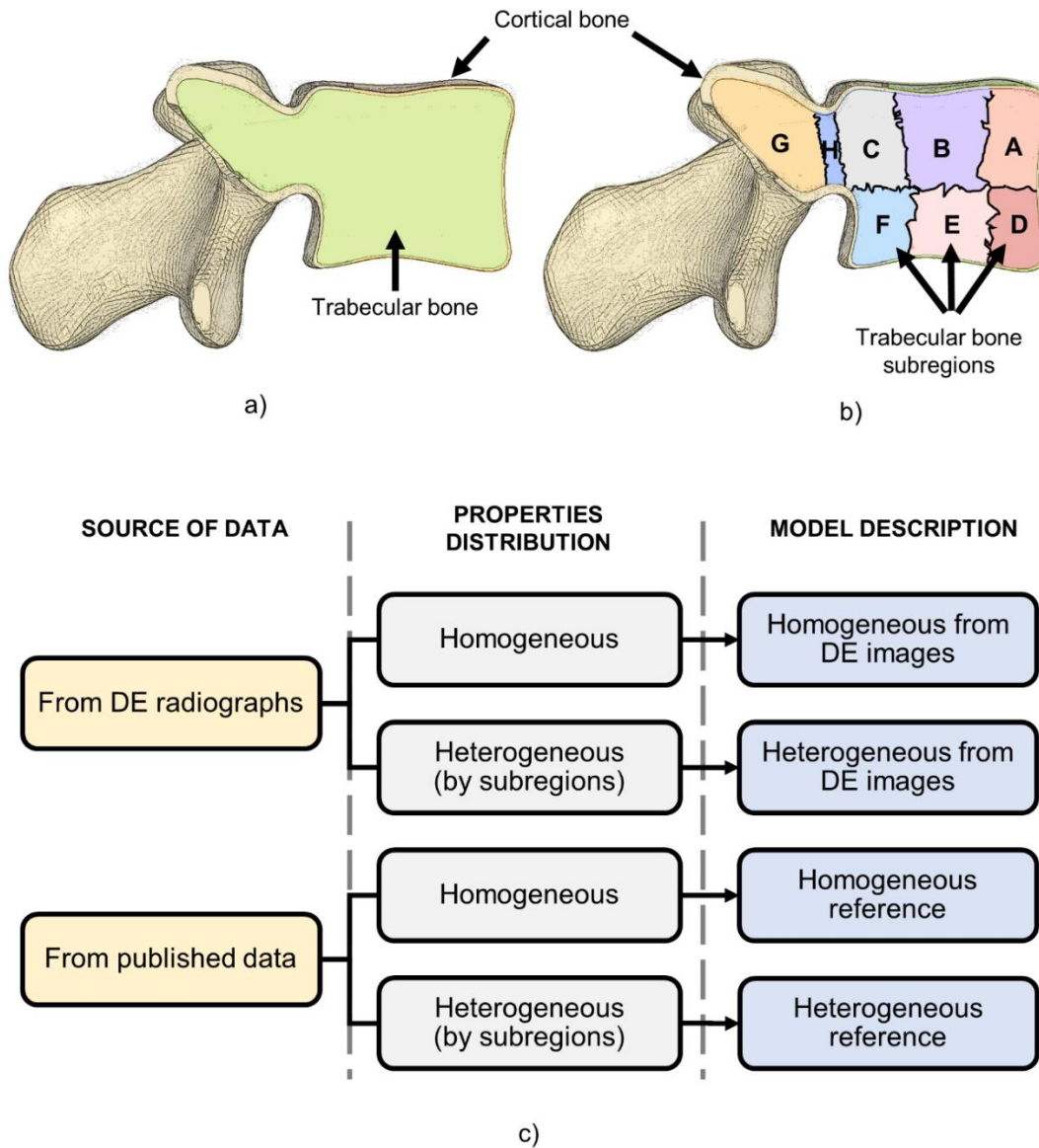


Figure 4.2 Isotropic FEMs of L3. a) A homogeneous model with both cortical and trabecular bone elements. b) A heterogeneous model with trabecular elements divided into 8 subregions and a cortical bone layer. The trabecular bone subregions are named A through H as follows: A) trabecular superior-anterior, B) trabecular superior-central, C) trabecular superior-posterior, D) trabecular inferior-anterior, E) trabecular inferior-central, F) trabecular inferior-posterior, G) trabecular posterior elements, and H) trabecular pedicle region. c) Diagram of the four vertebral models of this study

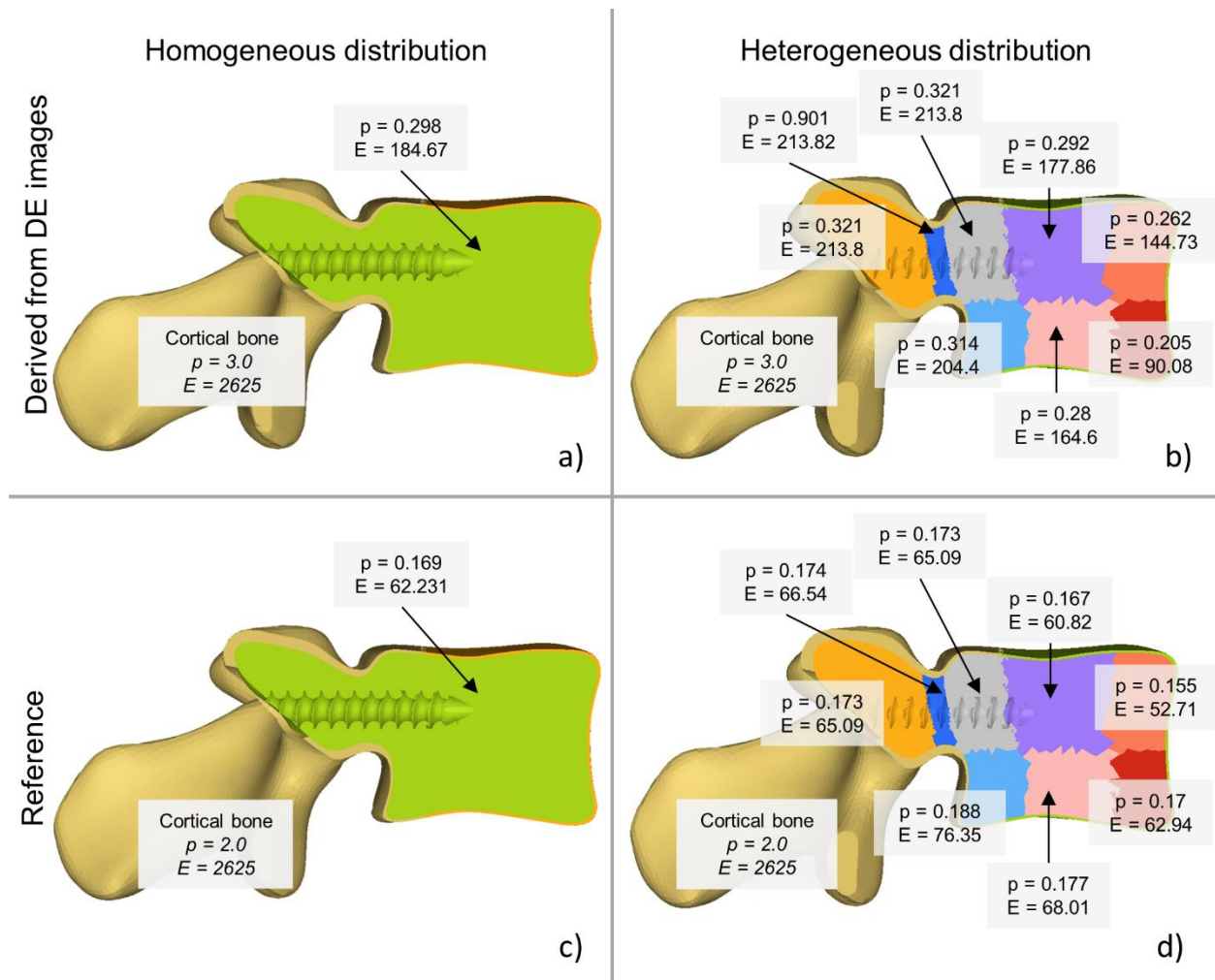


Figure 4.3 Mechanical properties of the four L3 vertebral models: a) homogeneous model from DE images, b) heterogeneous model from DE images, c) homogeneous reference model, and d) heterogeneous reference model. Values of volumetric bone mineral density ( $\rho$ , in  $\text{g}/\text{cm}^3$ ) and Young's modulus ( $E$ , in MPa) are shown over each region for trabecular and cortical bone

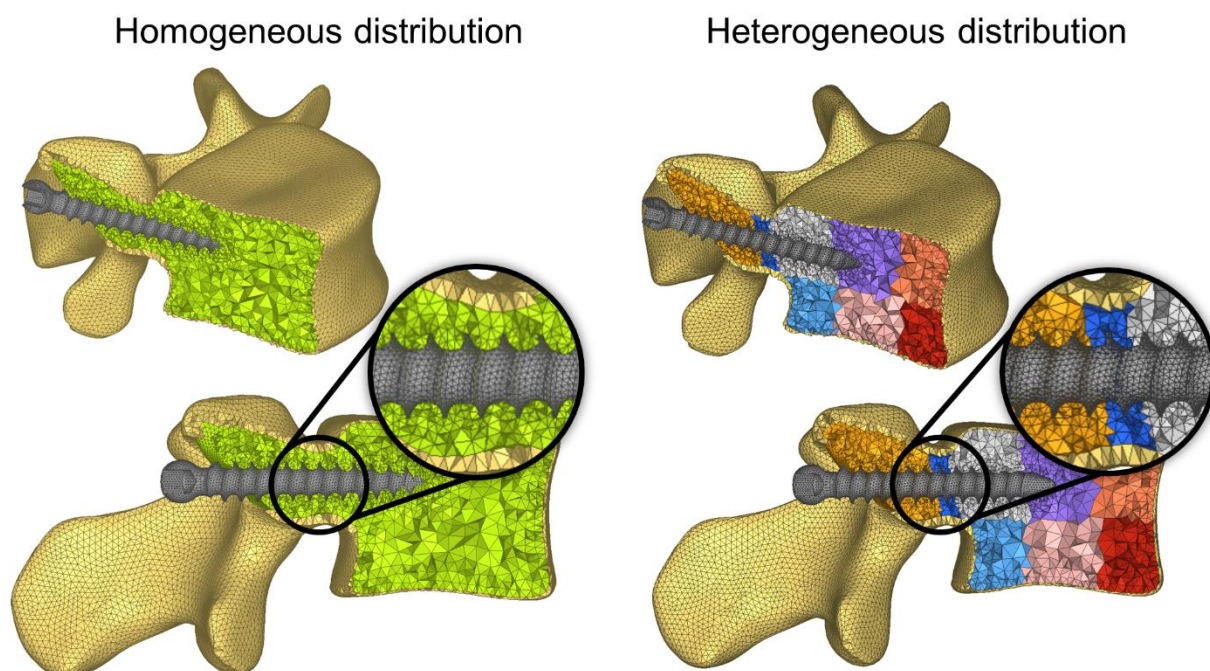


Figure 4.4 Meshed models with homogeneous and heterogeneous distribution with pedicle screw inserted in the right pedicle. Tetrahedral elements are seen in the trabecular bone surfaces. A closed-up view of the meshing between the screw model and the trabecular bone is displayed

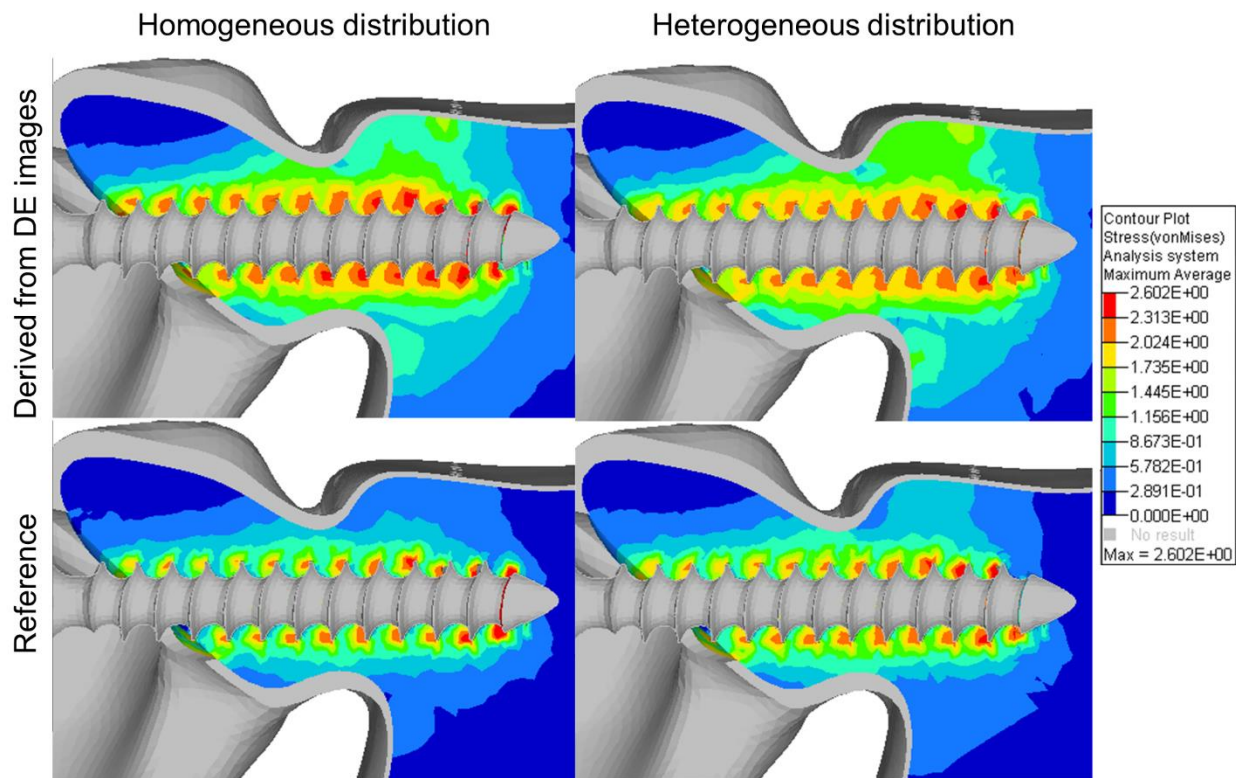


Figure 4.5 Von Mises stress distribution in the trabecular bone after the pedicle screw pullout simulation for the four models. A color-coded legend shows the maximum stress presented on the model elements, red as the maximum value to blue as the lowest value. Images were captured for each model at their own peak pullout force, which is manifested at a different time for each one

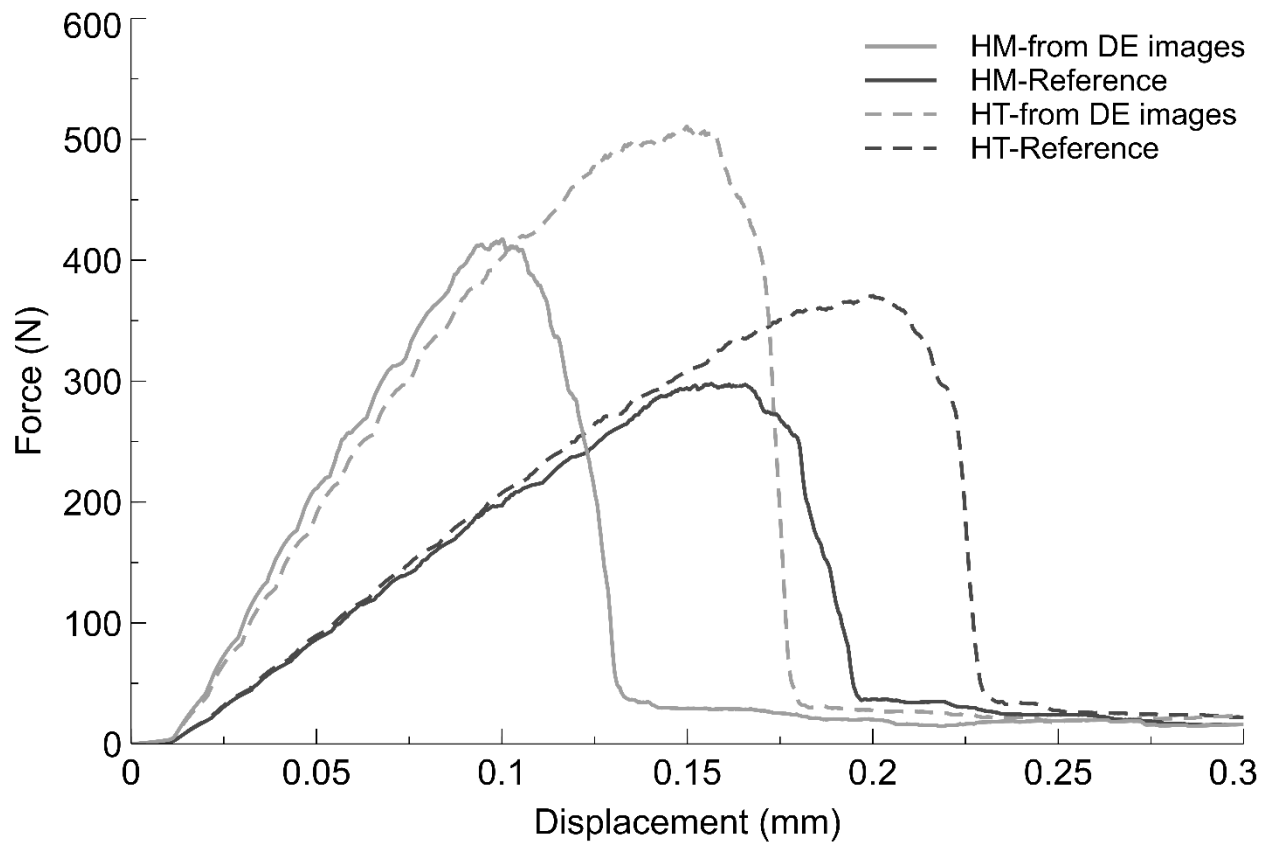


Figure 4.6 Force-displacement curves for all vertebral models. Models with properties derived from DE images (light grey) reach peak force at a smaller displacement, when compared to the reference (dark grey). Homogeneous models (HM) are shown in bold and heterogeneous models (HT) are shown with dashed lines

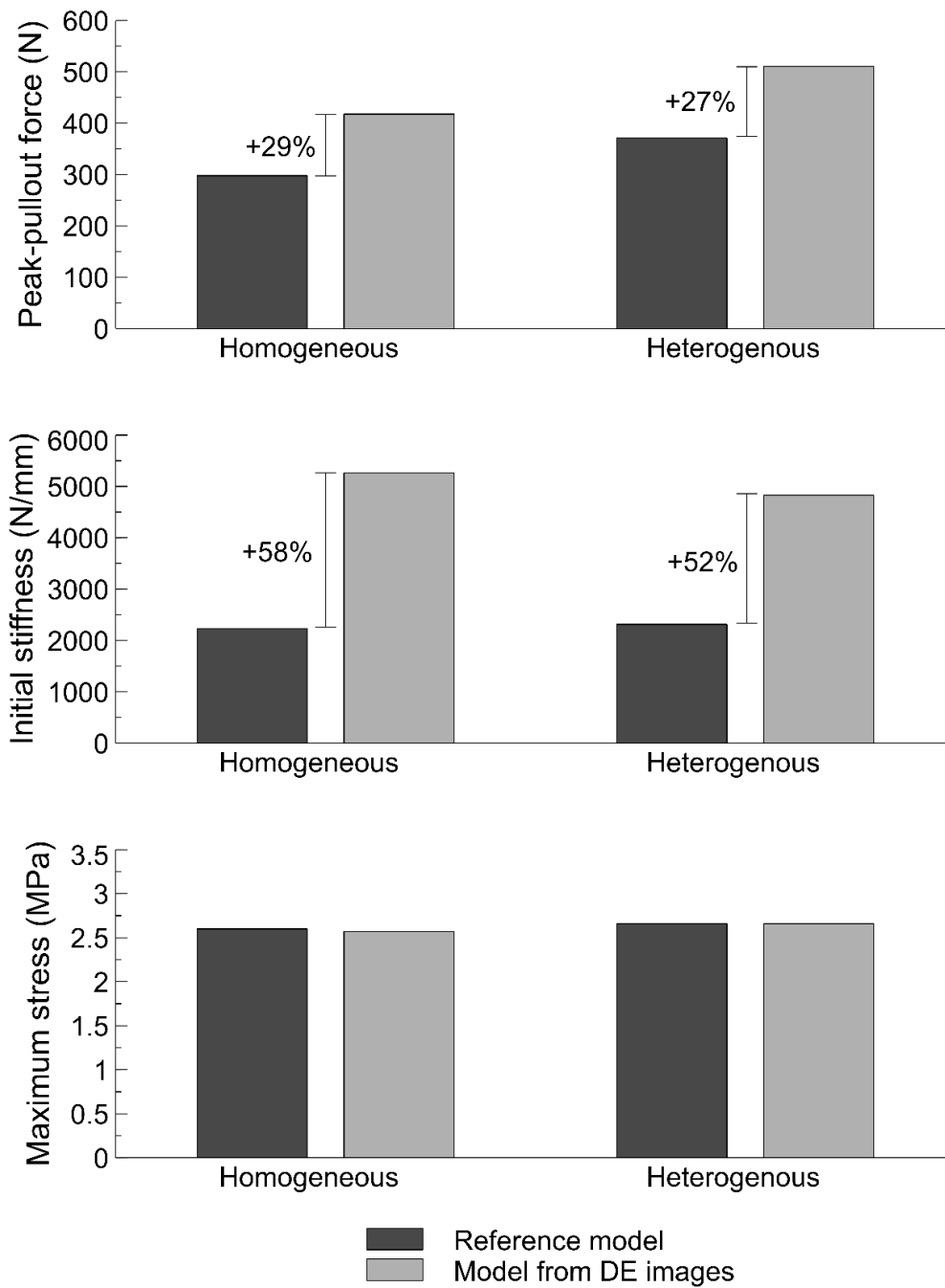


Figure 4.7 Simulation results of pedicle screw pullout for the homogeneous and heterogeneous models with properties derived from DE images (light grey) and reference models (dark grey). The increase in peak pullout forces and initial stiffnesses are reported. There was no difference for the maximum stress values

## **CHAPTER 5      ESTABLISHING A FRAMEWORK FOR AN L3 VERTEBRAL FINITE ELEMENT MODEL BASED ON PATIENT- SPECIFIC MECHANICAL PROPERTIES**

Following the methodology described in the research article presented in Chapter 4, additional information on this chapter will present the results of the influence from different elastic moduli into the heterogeneous patient-specific vertebral FEM, allowing an overview of the model's sensitivity.

As mentioned in section 2.2.3., previous experimental studies have presented mathematical relationships that relate bone mineral density and the elasticity modulus, or Young's modulus. These relationships can be either linear or power-law regressions and could depend on other parameters. The authors of four studies (Table 2.1) did experimental testing on different human vertebral segments to estimate mathematical regressions and obtain equations that relate the trabecular BMD and the Young's modulus (Figure 5.1).

For the heterogeneous model with mechanical properties derived from DE images (section 4.4.3.1), a series of preliminary processes were done to evaluate the performance of each Young's modulus resulting from the literature equations and analyze the results on pedicle screw pullout simulation. The objective of this section is to present a sensitivity study on the L3 vertebral FEM with heterogeneous distribution of different Young's moduli derived from four different equations presented in Table 2.1 during pedicle screw pullout simulation.

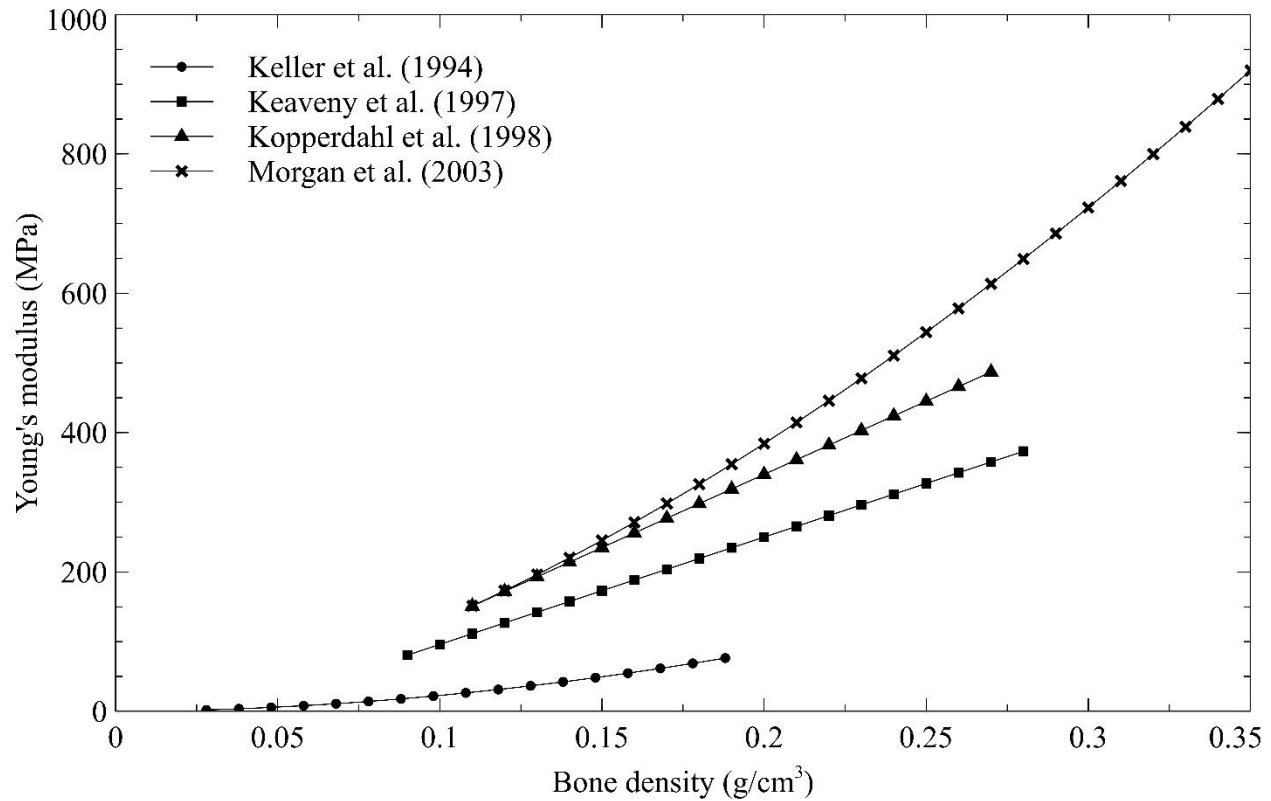


Figure 5.1 Regression from mathematical equations for Young's modulus as a function of bone apparent density from four experimental published studies.

## 5.1 Methodology

Volumetric bone mineral density was estimated from HA-density calibrated radiographs (section 4.4.3.1) for the heterogeneous models (Table 4.2). Using the four different equations (Table 2.1) to derive Young's modulus from vBMD, four vertebral FEMs were generated (Table 5.1). The mechanical properties derived from DE images into the four vertebral FEMs are presented in Table 5.2.

Table 5.1 Description of the four models for the Young's modulus sensitivity test.

| Model name | Model description                                                                          | Equation                |
|------------|--------------------------------------------------------------------------------------------|-------------------------|
| HT001      | Vertebral FEM with Young's modulus derived with the equation from Kopperdahl et al. (1998) | $E = 2.1\rho - 0.08$    |
| HT002      | Vertebral FEM with Young's modulus derived with the equation from Keaveny et al. (1997)    | $E = 1.540\rho - 0.058$ |
| HT003      | Vertebral FEM with Young's modulus derived with the equation from Keller (1994)            | $E = 1.89\rho^{1.92}$   |
| HT004      | Vertebral FEM with Young's modulus derived with the equation from Morgan et al. (2003)     | $E = 4.730\rho^{1.56}$  |

A simulation of pedicle screw pullout was performed as described in section 4.4.5.1 from the research article in Chapter 4. The peak pullout force and initial stiffness of the bone-screw interface were estimated with the force displacement curves of each model. The maximum stress distribution of the trabecular bone was estimated as the Von Misses stress distribution using the HyperView v2013 tool (Altair Engineering, 2013).

Correlation coefficients were estimated between all simulation parameters and the average Young's modulus estimated for each trabecular bone subregion for the four models using Excel 365 (Microsoft Office 365, 2021).

Table 5.2 Mechanical properties for heterogeneous vertebral FEMs with different Young's moduli derived from equations in the literature.

| Mechanical Properties           | Trabecular bone subregions |        |        |        |        |        |        |        | Cortical bone |
|---------------------------------|----------------------------|--------|--------|--------|--------|--------|--------|--------|---------------|
|                                 | A                          | B      | C      | D      | E      | F      | G      | H      |               |
| Density (g/cm <sup>3</sup> )    | 0.262                      | 0.292  | 0.321  | 0.205  | 0.280  | 0.314  | 0.321  | 0.901  | 2625          |
| Young modulus (MPa)             |                            |        |        |        |        |        |        |        |               |
| Models                          | HT001                      | 470.83 | 533.27 | 594.99 | 350.28 | 509.02 | 579.38 | 594.99 | 0.3           |
|                                 | HT002                      | 345.94 | 391.73 | 436.99 | 257.54 | 373.95 | 425.55 | 436.99 |               |
|                                 | HT003                      | 144.73 | 177.86 | 213.82 | 90.08  | 164.61 | 204.43 | 213.82 |               |
|                                 | HT004                      | 541.76 | 640.55 | 743.91 | 368.54 | 601.48 | 717.25 | 743.91 |               |
| Poisson ratio                   | 0.2                        | 0.2    | 0.2    | 0.2    | 0.2    | 0.2    | 0.25   | 0.25   |               |
| Yield stress (MPa)              | 1.651                      | 1.866  | 1.968  | 1.914  | 2.048  | 2.248  | 1.968  | 1.968  | 105           |
| Hardening modulus (MPa)         | 8.5                        | 7      | 8.5    | 8.1    | 12.5   | 12.5   | 7      | 7      | 875           |
| Hardening exponent              | 1                          | 1      | 1      | 1      | 1      | 1      | 1      | 1      | 1             |
| Failure plastic strain          | 0.082                      | 0.06   | 0.082  | 0.08   | 0.104  | 0.104  | 0.06   | 0.06   | 0.04          |
| Plasticity Maximum stress (MPa) | 2.65                       | 2.3    | 2.65   | 2.6    | 3.25   | 3.25   | 2.3    | 2.3    | 140           |

## 5.2 Results

The maximum stress distribution is concentrated around the screw threads on the trabecular bone for all models (Figure 5.2). For models with higher Young's modulus (HT001 and HT004), a much higher stress distribution is present in the posterior elements, the pedicles and the posterior superior and inferior regions of the vertebral body. There are specific areas that present high stress in the inferior region of the vertebral body and close to the junction with the pedicles. Model HT002 presents a slightly lower stress distribution in the bone compared to the two mentioned models, but still considerably higher than model HT003. The latter estimated a lower Young's modulus and thus presents lower stress distribution around the screw threads and the posterior regions of the vertebral body compared to the rest of the models. Maximum stress values however are all within the same range value of 2.6 MPa (Table 5.3).

The peak pullout forces for all models ranged between 511 to 640 N, with HT001 and HT004 having the highest values. The same tendency is seen for the initial stiffness of the bone-screw interface, with values ranging between 4644 to 9503 N/mm (Table 5.3).

Figure 5.3 shows the force-displacement curves for all models. Model HT003 (from Keller et al. (1994)) reached a peak pullout force at a larger displacement (0.15 mm) than the other models, which had similar results between them.

Table 5.3 Results for pedicle screw pullout simulation for the four heterogeneous models with different estimated Young's moduli (HT001-HT004).

| Simulation parameters    | HT001  | HT002  | HT003  | HT004  |
|--------------------------|--------|--------|--------|--------|
| Peak pullout force (N)   | 621.08 | 589.78 | 511.1  | 642.62 |
| Initial stiffness (N/mm) | 8538.4 | 7220.7 | 4644.1 | 9503.6 |
| Maximum stress (MPa)     | 2.655  | 2.661  | 2.665  | 2.656  |

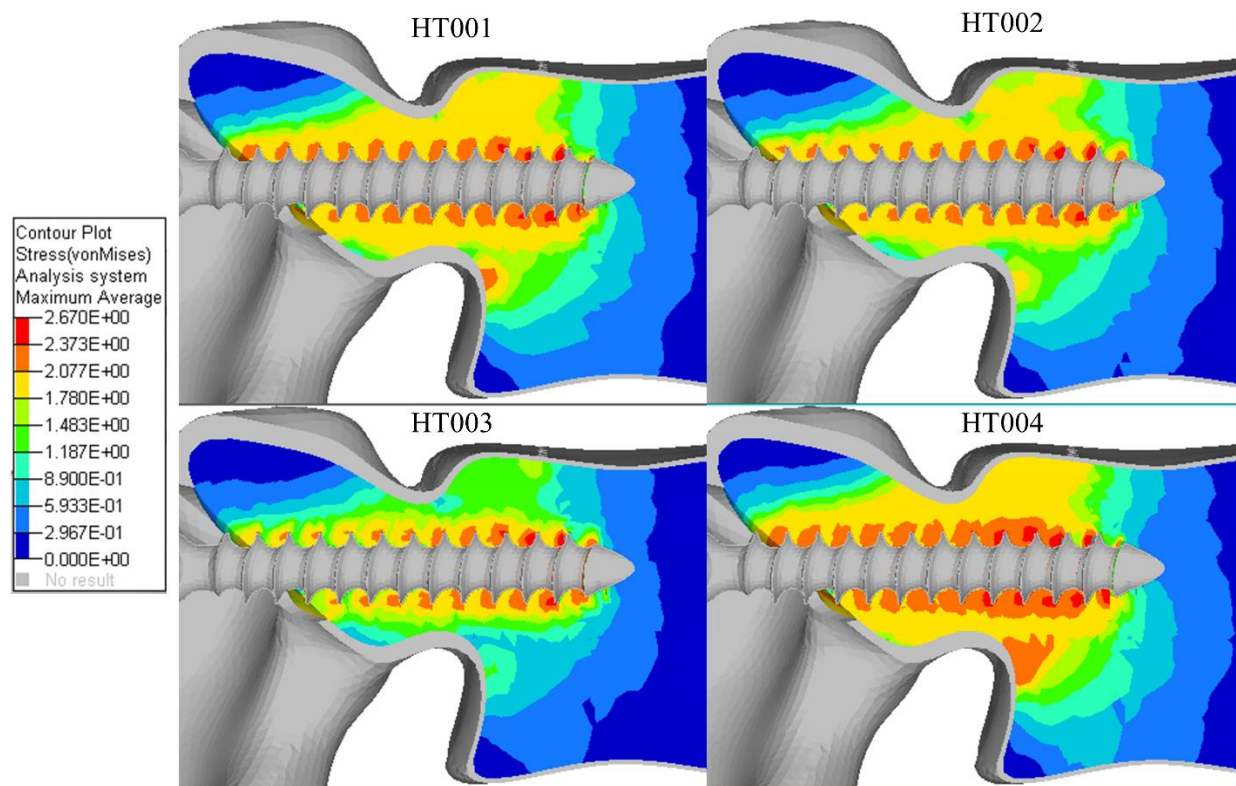


Figure 5.2 Stress distribution around the trabecular bone on the vertebral FEMs with different Young's modulus.

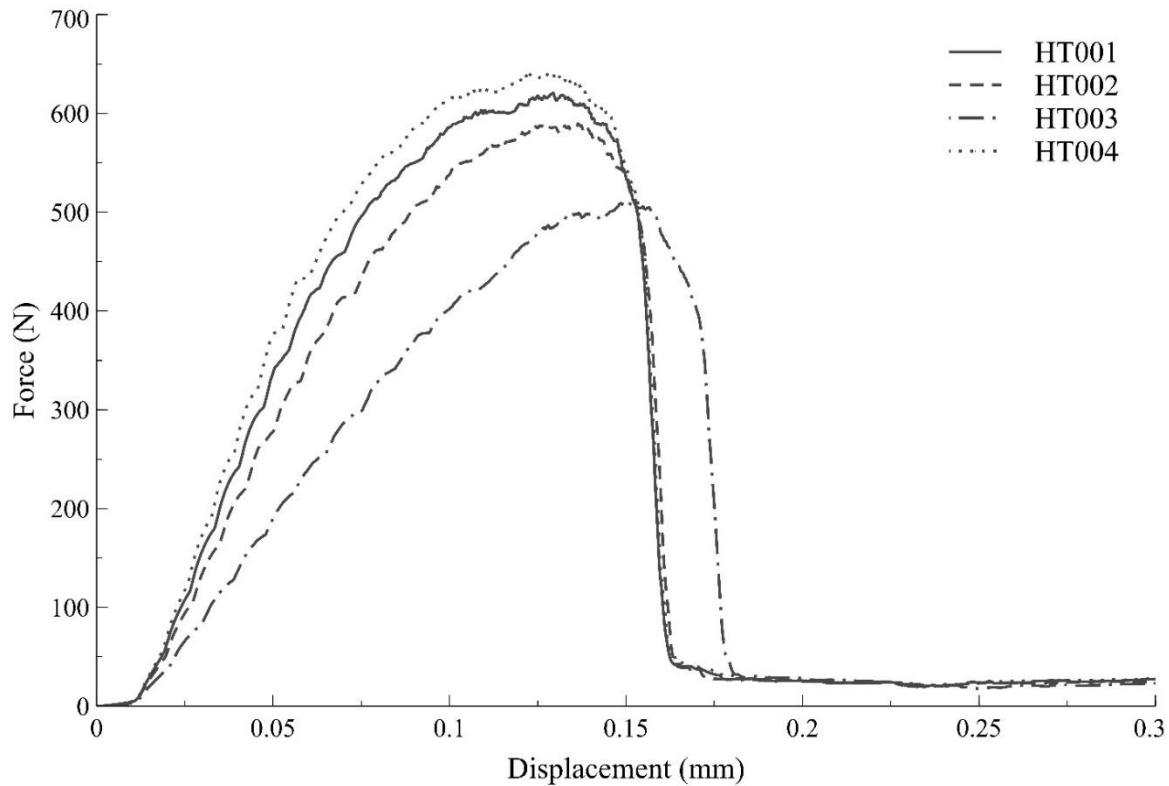


Figure 5.3 Force-displacement curves for the four vertebral FEMs with different estimated Young's moduli.

A high positive correlation was estimated for the average Young's modulus of each model and their corresponding results for peak pullout force ( $r = 0.998$ ) and initial stiffness ( $r = 0.996$ ). For the same parameter, a high negative correlation was estimated for the maximum stress distribution values ( $r = -0.946$ ) (Table 5.4).

Table 5.4 Correlation coefficients for pullout simulation parameters and models' average Young's modulus.

|                            | Peak pullout<br>force | Initial<br>stiffness | Maximum<br>stress | Average Young's<br>modulus |
|----------------------------|-----------------------|----------------------|-------------------|----------------------------|
| Peak pullout force         | 1.0                   |                      |                   |                            |
| Initial stiffness          | 0.9972                | 1.0                  |                   |                            |
| Maximum stress             | -0.9431               | -0.9476              | 1.0               |                            |
| Average Young's<br>modulus | 0.9880                | 0.9967               | -0.9461           | 1.0                        |

### 5.3 Discussion and Conclusion

The models with higher average trabecular bone Young's modulus (HT001 and HT004) presented high bone-screw interface stiffness and peak pullout force, and was confirmed with a high positive correlation. Bianco et al. (2017) presented numerical results with the same pedicle screw (6.5 x 40 mm) on the same type of L3 vertebral model (SM2S) where the stiffness ranged between 1327-4800 N/mm and the peak pullout force ranged between 220-750 N. Experimental work reports an initial stiffness range of 1100-2700 N/mm and peak pullout force range of 218-840 N (Abshire et al., 2001; Inceoglu et al., 2004; Mehta et al., 2012; Santoni et al., 2009). The values from HT001, HT004 and even HT002 greatly surpass the published ranges for initial stiffness only. Model HT003 results are within the range of the published numerical and experimental work for both parameters.

Additionally, several areas on the trabecular bone around the pedicle screw were greatly affected by high values of stress during the simulation for the HT001, HT002 and HT004 models, compared to the HT003 model. Model HT004 had a high stress distribution around the screw threads anchored in the posterior regions of the vertebral body as well as the inferior junction area between the pedicles and the vertebral body. Model HT003, on the other hand, presented much lower stress values around the screw threads. From this perspective, model HT003 possessed better mechanical properties to distribute appropriately the stress distribution around the pedicle screw during pullout simulation.

For the L3 vertebral FEM presented in this thesis, it was concluded that the equation presented from Keller et al. (1994) to relate trabecular bone vBMD and Young's modulus had the best performance on pedicle screw pullout simulation. Using this vBMD-modulus equation, appropriate results were achieved for the bone-screw interface initial stiffness and peak pullout force as well as good stress distribution around the screw threads. The vertebral FEM is sensitive to the assigned trabecular Young's modulus resulting in a significant change in the force-displacement curve and the stress distribution measurement.

## CHAPTER 6      GENERAL DISCUSSION

The presented work of this master's project has responded to the general objective of developing a vertebral FEM that integrates the mechanical properties estimated from a DE imaging system and of analyzing its feasibility to perform pedicle screw pullout simulations. Two main findings were identified:

- The method developed to estimate vBMD from bi-planar HA-calibrated radiographs and to derive mechanical properties from published equations is feasible for the scope of this study.
- The response to pedicle screw pullout simulation on a vertebral FEM depends on the integrated mechanical properties (high or low Young's modulus and bone mineral density) and their distribution within the trabecular bone (homogeneous or heterogeneous).

The low dose dual-energy imaging system is currently a novel technology where published studies are limited. The present study is the first to present a comprehensive analysis of the capabilities of the resulted DE radiographs. HA-calibrated radiographs suggest great potential to evaluate a patient's bone quality without compromising their health (such as in CT scans) or image quality (such as in DXA). Their limitation lies, as in other studies (Choisne et al., 2018; Humbert, L. et al., 2009; Humbert, Ludovic et al., 2017), on the complexity of integrating bi-planar images into a 3D perspective. In this work, a straightforward methodology was followed according to the work of Carter et al. (1992), in order to consider the volumes of the regions and subregions of the vertebral bone. The resulted values for vBMD were within acceptable range, confirming the feasibility of this technology to be used into estimating bone quality.

Moreover, different mathematical relationships relating vBMD and rigidity were evaluated on the L3 vertebral FEM (Chapter 5). As a result, the equation published by Keller et al. (1994) (Equation 4.1) was selected to be the best at estimating the elastic modulus without compromising high stress distribution on the trabecular bone. There is, however, a high inter-individual variability of the published relationships between vBMD and Young's modulus. Either cadaver or animal bone samples are used in experimental testing, and in humans, ages could vary between 18 to 85 years (Carter & Hayes, 1977; Helgason et al., 2008; Keaveny et al., 1997; Keaveny et al., 1994; Kopperdahl & Keaveny, 1998; Rice et al., 1988). This variation could have an impact on the

accuracy of the estimated Young's modulus in this study. In order to achieve more accurate results for a similar study, additional experimental testing should be included to derive mathematical regressions of vBMD and Young's modulus on a cadaveric sample and derive its properties as well with the DE imaging system, similar to Sapin de Broses et al. (2010). It is important to mention that the mechanical properties for the all the models were verified according to the definitions of the Johnson-Cook law.

The force-displacement curves of heterogeneous models with high and low rigidities (Figure 5.3) show the sensitivity of the model to these changes when performing pedicle screw pullout simulation. Higher rigidity values will have a tendency to increase the bone-screw interface stiffness and peak pullout force of the screw as seen in the correlation data from Table 5.4. A similar work was reported by Liu et al. (2014) where the pedicle region was analyzed and found that there is circular region around the screw that is sensitive to the material properties of trabecular bone. The trabecular bone zones closer to the screw threads will likely present higher stress values, and even more for a higher rigidity, as did the results of the present study (Figure 5.2). These findings highlight how specific subregions of the trabecular bone can affect the sensitivity of a vertebral FEM during pedicle screw pullout simulations, with not only their position (vertebral body, pedicles) but their material properties (vBMD and rigidity). These subregions, however, only represent important variations of BMD within the vertebral body, the pedicles, and the posterior elements. For pedicle screw insertion, smaller subregions closer and around the screw threads as well as throughout the screw length could show different results during pullout simulation and these changes should be considered for further research.

Moreover, the results showed in Chapter 4 also demonstrate the model's sensitivity to the distribution of trabecular bone properties. The heterogeneous models presented higher pullout forces regardless of their properties' origin. However, only for the heterogeneous model with properties derived from DE images, the stiffness and stress distribution around the screw threads decreased compared to the homogeneous model. Having a cohesive distribution of the mechanical properties – increasing value of the properties from the posterior regions of the vertebral body to the pedicles and posterior elements – allows the vertebrae to withstand the stress of axial pedicle screw pullout.

This work presents certain limitations regarding the methodology of estimating the vBMD from bi-planar DE radiographs, as mentioned in section 4.6. There is a need for an automatic process to accurately estimate the ROIs that differentiate: 1) the trabecular and cortical bone, and 2) the subregions of the trabecular bone. 3D reconstructions of the spine can be generated using the bi-planar radiographs. With the proper functions, a binary mask in the shape of each vertebra over the HA-calibrated radiographs could be formed to estimate an average pixel value (which is calibrated in  $\text{g}/\text{cm}^2$  in this case) of the trabecular and cortical bone, allowing an estimation of vBMD for the homogeneous model. However, for the heterogeneous model, where subregions must be selected within the trabecular bone surfaces, the process is more complicated and thus requires manual selection. Additionally, due to the tissue overlapping generated on the bi-planar radiographs, there could be an overestimation of the vBMD, specially in certain areas such as the pedicle regions in the PA views. Sapin de Brosses et al. (2010) mentioned how the estimated areal BMD from the LAT view better correlated with their measured apparent density on thoracic vertebrae, than with the area BMD from the PA view. Indeed, for this project, all estimations done with LAT views resulted more within acceptable range (from the literature) and subregions were easier to manually select than estimations from PA views. Future research should focus on creating an automatic algorithm to process the generated bi-planar radiographs to 1) differentiate pixel selection from cortical and trabecular bone, 2) select trabecular bone subregions for the heterogeneous model and 3) directly estimate the vBMD for each subregion.

The methodology presented in this study could assist to evaluate the bone quality of *in vivo* vertebrae and other bone structures using the DE imaging system. Detailed analysis of the bone structure is possible with the contour-enhanced radiographs provided by the system (not the image simulator) and bone quality can be assessed with HA-calibrated radiographs. This allows its use for bone quality assessment for orthopedic surgical planning (pre- and post-op). For adults with spinal deformities, bone quality is generally decreased (osteoporosis) and thus requires additional attention to risk factors for the application of orthopedic implants. Integration of the mechanical properties of the bone into a FEM, regardless of the anatomical section, could assist to provide surgeons which surgical option would have the best outcome and decrease pedicle screw failure.

Due to the advantage of the DE imaging system and the findings of this study, it is suggested that further research focuses on exploring the capabilities of the other calibrated radiographs, such as the PMMA-calibrated radiographs, and their potential application in a FEM.

## CHAPTER 7 CONCLUSION AND RECOMMENDATIONS

In this research study, an L3 vertebral FEM that integrates the mechanical properties of the bone tissue was developed using DE radiography in the context of pedicle screw fixation. Volumetric bone mineral density was derived using the DE imaging system which provided hydroxyapatite density-calibrated radiographs and rigidity values were estimated using published mathematical relationships. The model was compared to an equivalent model with properties derived from published data to assess the difference of patient-specific and generalized mechanical properties. In order to represent realistic parameters on the model, two different distributions of the trabecular bone were integrated in the FEM: homogeneous and heterogeneous. Pedicle screw pullout simulation was performed where the peak pullout force, maximum internal stress distribution and bone-screw interface initial stiffness were measured. Models with properties derived from DE images had higher measured values than the reference models for all parameters. However, the heterogeneous model with properties derived from DE images presented less stress distribution around the screw threads and decreased stiffness. A better resistance is observed on the first quarter of the pedicle screw length due to proper distribution of the mechanical properties of the trabecular bone in the heterogeneous model. This model was demonstrated to be feasible in the scope of pedicle screw fixation when integrating patient-specific mechanical properties derived from DE radiographs.

The specific objective 1 was achieved with the methodology to generate DE radiographs and to estimate the vBMD. The second specific objective was achieved in Chapter 5 by evaluating multiple mathematical relationships that relate vBMD and rigidity. Finally, the specific objective 3 was achieved by performing pedicle screw pullout simulations on all models and evaluating their outcomes.

Although the methodology of this study is simple, it presented an insight into the capabilities of the DE imaging system and the feasibility of integrating patient-specific properties into a vertebral FEM. Future research should focus on exploring these capabilities for applications not only in the spine but other bone structures or tissues. The following recommendations of future work are proposed:

- Development of an algorithm to process the dual-energy radiographs in order to identify with detail the different subregions of trabecular and cortical bone, and thus estimate volumetric bone mineral density, following the methodology presented in this study.
- Development of a study to evaluate the feasibility and validate this project with 1) a selected patient dataset on either healthy or pathological vertebrae (i.e., low vBMD), and 2) the integration of the vertebral geometry into the FEM.
- Development of a study to explore the capabilities of the PMMA-calibrated radiographs provided by the DE imaging system and further assess the characteristics of soft tissues of the spine (i.e., intervertebral discs) or other anatomical regions.
- Development of a study to continue the evaluation of pedicle screw fixation on heterogeneous vertebral FEMs with patient-specific mechanical properties using different pedicle screw dimensions and trajectories.

This study demonstrated how patient-specific mechanical properties could affect the performance of orthopedic simulation in finite element modeling. With the growing interest of patient-specific modeling, further research on the novel DE imaging system is encouraged for its capability on the assessment of bone quality using low-dose radiation.

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## APPENDIX A    MANUAL ESTIMATION OF PATIENT-SPECIFIC VOLUMETRIC BONE DENSITY FROM BI-PLANAR BONE- CALIBRATED RADIOGRAPHIC IMAGES

Dual-energy radiographic images were used to estimate the volumetric bone mineral density of the vertebrae. Using ImageJ measuring tools, the trabecular bone subregions were measured and with a series of geometrical calculations, the volumetric bone density was estimated for the model with heterogeneous distribution (section 4.4.2.1).

For the lateral view of the radiographic image of the test case, six subregions (1-6) were manually selected using ImageJ ROI manager tool, representing respectively the superior-anterior, superior-central, superior-posterior, inferior-anterior, inferior-central, and inferior-posterior regions (Figure A.1). Using the Measure tool in ImageJ, the ROI parameters were measured such as the area, mean pixel value, minimum and maximum pixel values, etc. For this study, only the area ( $\text{cm}^2$ ) and the mean pixel value (calibrated in  $\text{g}/\text{cm}^2$ ) were used.

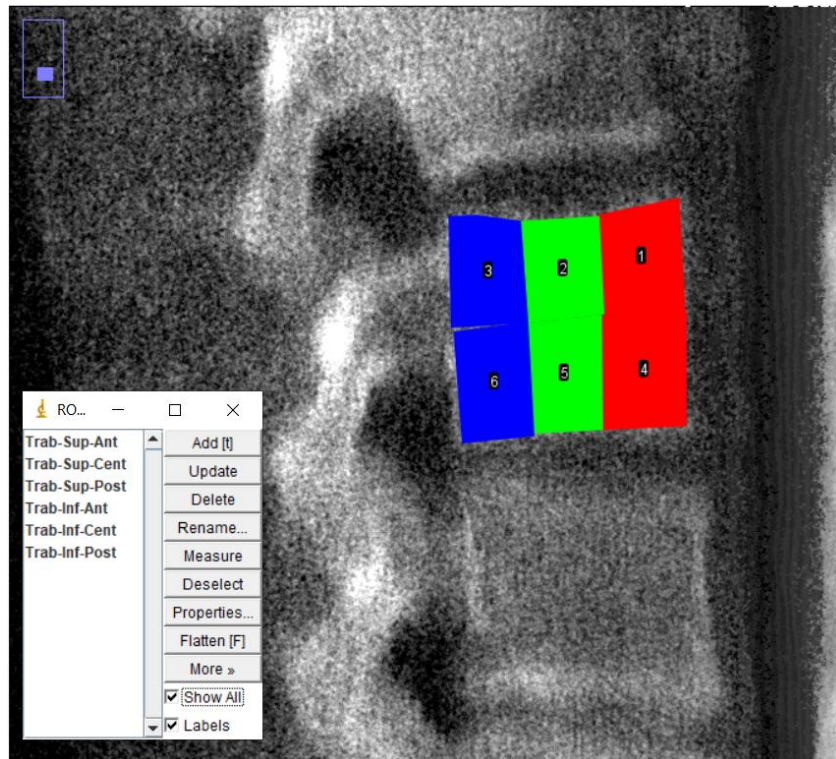


Figure A.1 Selected ROIs in the lateral view of the DE radiograph of the test case for L3. The labels 1 to 6 respectively correspond to the subregions defined in the left side of the figure.

The procedure to estimate volumetric bone mineral density from the obtained measurements on the radiographic images was obtained from the work of Carter et al. (1992), which is described as such:

1. Estimate bone mineral content (BMC) from the region area and BMD:  $BMC = BMD * Area$
2. Measure the depth (cm) of the vertebral body for each view using ImageJ measure tool on a manually defined line (Figure A.2).
  - a. Consider a rectangular prism for each subregion of the vertebral body.
  - b. Consider a cylindrical prism for the pedicle regions.
3. Estimate the volume of the subregion with the area and the vertebral body depth for each view:  $Volume = Area * Depth$ .
4. Estimate the volumetric bone mineral density (vBMD) with the subregion volume and BMC:  $vBMD = BMC/Volume$ .

Table A.1 shows the resulted values for the estimation of each subregion parameter and the resulted vBMD for each trabecular bone subregion in the lateral and posteroanterior view. Note that the estimated value for vBMD of each subregion in the posteroanterior view is considerably higher than of the lateral view. This is likely to be due to the large area that is considered from the PA view, which consequently overestimates the mean pixel value due to tissue overlapping (the vertebral body over the pedicles and posterior elements). Therefore, four samples of each corner of the trabecular bone radiographic image in the PA view were taken to correctly estimate the vBMD (Table A.2). The resulted vBMD is therefore considered at the estimated vBMD for the PA views on Table A.1 for each subregion. Table A.3 presents the results for the pedicle regions following the same process described above.

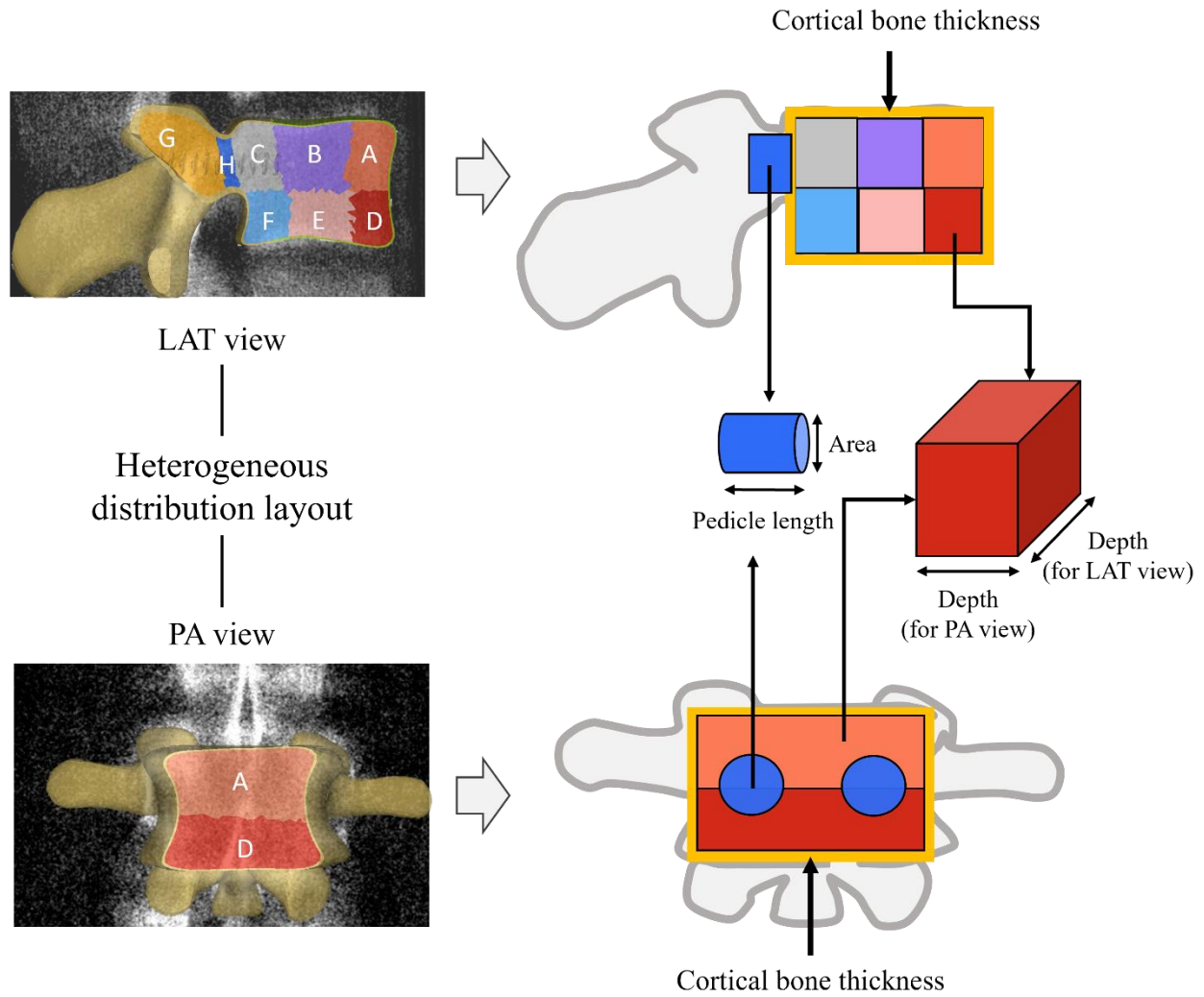


Figure A.2 Representation of the measurements taken on the DE radiographs (LAT and PA) using ImageJ measurement tools.

Table A.1 Geometrical measurements for the heterogeneous model trabecular bone subregions. Results highlighted in light grey were obtained from ImageJ measuring tool. Results highlighted in dark grey were obtained from Table A.2. Results in bold were the final estimated vBMD used in the methodology of this study.

| Superior regions of the vertebral body |         |        |              |          |        |              |          |        |              |
|----------------------------------------|---------|--------|--------------|----------|--------|--------------|----------|--------|--------------|
| Geometrical measurements               | SUP-ANT |        |              | SUP-CENT |        |              | SUP-POST |        |              |
|                                        | LAT     | PA     | Both views   | LAT      | PA     | Both views   | LAT      | PA     | Both views   |
| Area (cm <sup>2</sup> )                | 2.226   | 8.465  |              | 1.932    | 8.465  |              | 2.008    | 8.465  |              |
| Mean pixel value (g/cm <sup>2</sup> )  | 0.656   | 1.286  |              | 0.916    | 1.286  |              | 1.173    | 1.286  |              |
| BMC (g)                                | 1.461   | 10.886 | 6.173        | 1.770    | 10.886 | 6.328        | 2.356    | 10.886 | 6.621        |
| Depth (cm)                             | 4.372   | 1.239  |              | 4.372    | 1.239  |              | 4.372    | 1.239  |              |
| Volume (cm <sup>3</sup> )              | 9.735   | 10.484 | 10.109       | 8.449    | 10.484 | 9.466        | 8.781    | 10.484 | 9.633        |
| vBMD (g/cm <sup>3</sup> )              | 0.150   | 1.038  | 0.594        | 0.209    | 1.038  | 0.624        | 0.268    | 1.038  | 0.653        |
| Total vBMD                             | 0.150   | 0.375  | <b>0.262</b> | 0.209    | 0.375  | <b>0.292</b> | 0.268    | 0.375  | <b>0.321</b> |
| Inferior regions of the vertebral body |         |        |              |          |        |              |          |        |              |
| Geometrical measurements               | INF-ANT |        |              | INF-CENT |        |              | INF-POST |        |              |
|                                        | LAT     | PA     | Both views   | LAT      | PA     | Both views   | LAT      | PA     | Both views   |
| Area (cm <sup>2</sup> )                | 2.402   | 7.366  |              | 2.012    | 7.366  |              | 2.066    | 7.366  |              |
| Mean pixel value (g/cm <sup>2</sup> )  | 0.535   | 1.352  |              | 1.196    | 1.352  |              | 1.489    | 1.352  |              |
| BMC (g)                                | 1.285   | 9.959  | 5.622        | 2.407    | 9.959  | 6.183        | 3.076    | 9.959  | 6.517        |
| Depth (cm)                             | 4.372   | 1.239  |              | 4.372    | 1.239  |              | 4.372    | 1.239  |              |
| Volume (cm <sup>3</sup> )              | 10.503  | 9.123  | 9.813        | 8.799    | 9.123  | 8.961        | 9.033    | 9.123  | 9.078        |
| vBMD (g/cm <sup>3</sup> )              | 0.122   | 1.092  | 0.607        | 0.274    | 1.092  | 0.683        | 0.341    | 1.092  | 0.716        |
| Total vBMD                             | 0.122   | 0.287  | <b>0.205</b> | 0.274    | 0.287  | <b>0.280</b> | 0.341    | 0.287  | <b>0.314</b> |

Table A.2 Geometrical measurements for the samples taken on the trabecular bone from the PA view. Results highlighted in light grey were obtained from ImageJ measuring tool.

| Geometrical measurements              | Inferior regions |       |       |       |       | Superior regions |       |       |
|---------------------------------------|------------------|-------|-------|-------|-------|------------------|-------|-------|
| Sample                                | 1                | 2     | 3     | 4     | 5     | 6                | 7     | 8     |
| Area (cm <sup>2</sup> )               | 0.120            | 0.085 | 0.102 | 0.086 | 0.085 | 0.115            | 0.077 | 0.063 |
| Mean pixel value (g/cm <sup>2</sup> ) | 0.907            | 0.725 | 1.050 | 1.590 | 1.981 | 1.034            | 0.870 | 1.682 |
| BMC (g)                               | 0.109            | 0.062 | 0.108 | 0.137 | 0.168 | 0.119            | 0.067 | 0.107 |
| Depth (cm)                            | 3.716            | 3.716 | 3.716 | 3.716 | 3.716 | 3.716            | 3.716 | 3.716 |
| Volume (cm <sup>3</sup> )             | 0.445            | 0.317 | 0.381 | 0.320 | 0.315 | 0.428            | 0.285 | 0.236 |
| vBMD (g/cm <sup>3</sup> )             | 0.244            | 0.195 | 0.283 | 0.428 | 0.533 | 0.278            | 0.234 | 0.453 |
| Average vBMD                          | 0.287            |       |       |       |       | 0.375            |       |       |

Table A.3 Geometrical measurements for the pedicle region. Results highlighted in light grey were obtained from ImageJ measuring tool.

| Geometrical measurements of the pedicle regions to calculate pedicle volume |       |            |           |            |
|-----------------------------------------------------------------------------|-------|------------|-----------|------------|
| Pedicle length (cm)                                                         |       |            | 1.141     |            |
| Area right (cm <sup>2</sup> )                                               |       |            | 0.663     |            |
| Area left (cm <sup>2</sup> )                                                |       |            | 0.684     |            |
| Volume of left pedicle (cm <sup>3</sup> )                                   |       |            | 0.780     |            |
| Volume of right pedicle (cm <sup>3</sup> )                                  |       |            | 0.757     |            |
| Average volumes (used for LAT view)                                         |       |            | 0.768     |            |
| Geometrical measurements of the pedicle regions to estimate vBMD            |       |            |           |            |
|                                                                             | LAT   | PA (Right) | PA (Left) | Both views |
| Area (cm <sup>2</sup> )                                                     | 0.946 | 0.663      | 0.684     |            |
| Mean pixel value (g/cm <sup>2</sup> )                                       | 1.038 | 0.930      | 1.212     |            |
| BMC (g)                                                                     | 0.982 | 0.617      | 0.476     | 0.692      |
| Volume (cm <sup>3</sup> )                                                   | 0.768 | 0.757      | 0.780     | 0.768      |
| vBMD (g/cm <sup>3</sup> )                                                   | 1.278 | 0.815      | 0.610     | 0.901      |

## APPENDIX B ESTIMATION OF VOLUMETRIC BONE MINERAL DENSITY FOR THE REFERENCE VERTEBRAL MODEL WITH PUBLISHED DATA

Banse et al. (2001) reported estimated volumetric bone mineral density for different subregions of the vertebral body from 48 cylindrical samples of 8 lumbar vertebrae. These subregions were categorized as anterior, posterior, and external (Figure B.1a). Four slices were cut transversely into these samples to analyze their microstructure. Additional subregions representing the upper and lower sections of the vertebral body were obtained with these cuts, categorizing them from 1 to 4 (Figure B.1b). Table B.1a shows the resulting values from this work.

In order to coincide the regions established by Banse et al. (2001) and the presented work, an approach of average by subregion was used. Table B.1b shows the results of the estimated vBMD for the heterogeneous model derived from the published work of Banse et al. (2001).

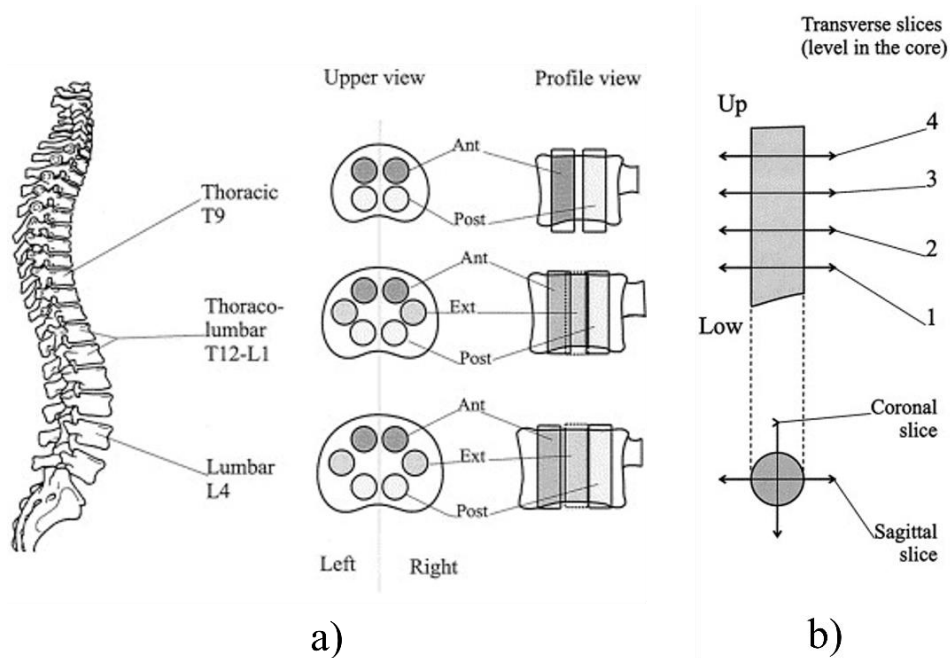


Figure B.1 a) Anterior, posterior, and external cylindrical samples taken from thoracolumbar vertebrae bodies. b) Transverse cuts made on each cylindrical sample to measure vBMD from upper to lower sections. From “Inhomogeneity of human vertebral cancellous bone: systematic density and structure patterns inside the vertebral body”, by X. Banse, J.P. Devogelaer et al., 2001, Bone, 28, p. 564-565. Copyright (2001) by Elsevier. Adapted with permission.

Table B.1 a) Volumetric bone mineral density from the work of Banse et al. (2001) which was used to b) corroborate and estimate the vBMD to use in the present work. Results in bold were used on the methodology presented in this study.

| a) Reported work of Banse et al. (2001)      |           |                              | b) Process of subregion correlation for the present work |       |                                          |                         |                              |
|----------------------------------------------|-----------|------------------------------|----------------------------------------------------------|-------|------------------------------------------|-------------------------|------------------------------|
| Categorization of trabecular bone subregions |           |                              |                                                          |       | Resulted estimation for the present work |                         |                              |
| Subregion of the vertebral body              |           | Density (g/cm <sup>3</sup> ) | Averaged subregions for upper and lower sections         |       | Selected subregions from published data  | Present work subregions | Density (g/cm <sup>3</sup> ) |
|                                              | Anterior  | 0.156                        |                                                          |       | Anterior & Superior                      | SUP-ANT                 | <b>0.155</b>                 |
|                                              | External  | 0.159                        |                                                          |       | Anterior & Superior & Posterior          | SUP-CENT                | <b>0.167</b>                 |
|                                              | Posterior | 0.192                        |                                                          |       | Posterior & Superior                     | SUP-POST                | <b>0.173</b>                 |
| Superior                                     | 4         | 0.152                        |                                                          |       | Anterior & Inferior                      | INF-ANT                 | <b>0.170</b>                 |
|                                              | 3         | 0.156                        | 4&3 - Superior                                           | 0.154 | Anterior & Inferior & Posterior          | INF-CENT                | <b>0.177</b>                 |
|                                              | 2         | 0.191                        |                                                          |       | Posterior & Inferior                     | INF-POST                | <b>0.188</b>                 |
| Inferior                                     | 1         | 0.177                        | 2&1 - Inferior                                           | 0.184 |                                          |                         |                              |