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EXECUTIVE SUMMARY OF THE THESIS

Dual Energy X-ray Absorptiometry: Mini Health Technology Assessment for Innovation in Technology within Santagostino Medical Centre

TESI MAGISTRALE IN BIOMEDICAL ENGINEERING – INGEGNERIA BIOMEDICA

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1. Introduction

For the purpose of this project, it has been carried out a Health Technology Assessment for the evaluation of the clinical effectiveness of an innovative Dual Energy X-ray Absorptiometer, considered as a standard typology of examination for the diagnosis of osteoporosis and other endocrinologic diseases. Osteoporosis is an emerging medical and socioeconomic threat characterized by a systemic impairment of bone mass, strength, and microarchitecture, which increases the propensity of fragility fractures. It affects more than 75 million people in Europe, Japan and the USA, and causes more than 2.3 million fractures annually in Europe and the USA alone. An expert panel of the World Health Organization (WHO) recommended thresholds to divide among different categories of patient at risk of osteoporosis, according to Bone Mineral Density (BMD) measurements, and proposed the DXA examination at the hip as the standard technology for the evaluation of an osteoporotic condition.
In this project, a Multi Criteria Decision Analysis has been performed in order to attribute a score to the technologies that were under the assessment for the introduction of the new bone densitometer in the company where the internship was carried out. Santagostino Medical Centre is a network of health clinics founded in 2009 with the objective to cover the growing needs of a large catchment area of patients: high quality medical services combined with the possibility to have an easy access to the available services thanks to fair prices. With the choice of the new machine, a subsequent on-site installation and technology configuration in "Repubblica" center was taken out. Of course, with the objective to optimize time and associated costs related to the company, it was scheduled an operating plan before the installation of the new DEXA technology. Moreover, a training of the technical and medical personnel was carried out to ensure a correct workflow for the exam execution, and consequently a production of a valuable report. Physicians, also, were trained with the aim

to provide guidelines on the correct use of threshold values for the discrimination among different conditions. Specialists in endocrinology, supported by the clinical opinion of the CMS health director, have presented, as a project for the new clinical offering for 2022, the intention to introduce newer technologies in the field of densitometry. The clinical requirement to be satisfied were concerned about the introduction of innovative software for the execution of textural measurements, in order to acquire information not only about bone quantity, but also regarding bone quality and applied loads. For these reasons, software integration was considered as a target tool to be adopted in this innovation.

2. Dual X-ray absorptiometry: State of the Art

Dual-Energy X-ray absorptiometry uses subtraction of multiple scans to obtain estimates of the Bone Mineral Density (BMD) and fat content. A soft tissue absorption image is subtracted from a higher energy bone image in order to estimate bone density with a high degree of accuracy. A typical DEXA scan acquisition consists of more than 10.000 individual measurement points (pixels), each one containing both spatial and consequent bone density information related to the intensity of the arrival photons in that specific unit.

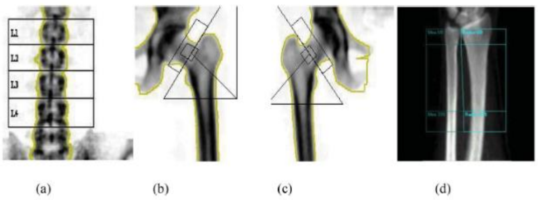


Figure 1: Examples of DEXA scan image (a) spine with vertebrae numbering (b) right femur (c) left femur (d) forearm.

2.1 Bone Mineral Density (BMD)

Assessment of bone mass, mostly termed as Bone Mineral Density (BMD), is the standard method for the definition of a diagnostic approach for an osteoporotic fracture risk evaluation. In [1], it was presented a model for the calculation of the apparent volumetric bone mineral density (BMD_{Vol}), since DXA scanning is projected to give as output 2D images, not volume reconstruction: therefore, indirect measurements are required (Figure 2). Always in [1], it was tested the validity

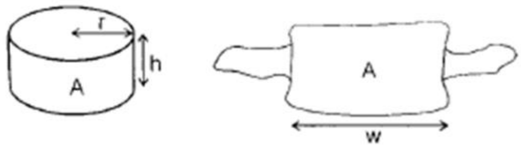


Figure 2: Model for the calculation of volumetric bone mineral density (BMD_{vol}) using DXA data

of the proposed model with the use of magnetic resonance imaging (MRI) for the measurement of the vertebral dimension. As a result, the precision error (coefficient of variation, CV) of the method for the measurement of the vertebral volume, based on three consecutive measurements on ten subjects, was 1.0%.

The lumbar body was assumed to have a cylindrical shape: the volume of the cylinder and BMD_{Vol} were calculated as follows:

$$Vol = \pi r^2 h = \pi \frac{wA}{4}$$

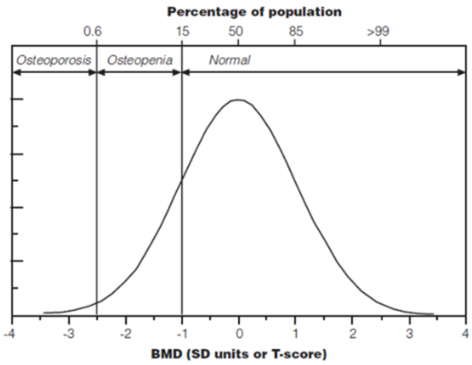
$$BMD_{vol} = \frac{BMC}{Vol} = BMD_A \frac{4}{\pi w}$$

Where $w =$ mean width of the vertebral body and A = mean area of vertebral body.

T-score of the BMD is then calculated by taking the difference among the patient's measured BMD and the mean BMD of the young normal population, and then by dividing this difference with the standard deviation (SD) of the BMD of the young normal population. The Z-score is similarly calculated, by comparing the patient with his/her age matched group.

$$T - score = \frac{\lambda - \mu}{\sigma}$$

$$Z - score = \frac{\lambda - \beta}{\alpha}$$



Graph 1: Distribution of BMD in young healthy women aged 30-40 years.

2.2 Trabecular Bone Score (TBS)

The diagnosis of osteoporosis with DXA suffers from the lack of any evaluation of the 3D microarchitecture of bone tissue, which constitutes an important component of bone strength. To meet the need for a clinical tool capable of assessing bone microarchitecture, the Trabecular Bone Score (TBS) was developed. As cited in [2], TBS has emerged as "[…] a novel grey-level texture measurement that uses experimental variograms of 2D projection images, quantifying variation in grey-level texture from one pixel to the adjacent pixels". The TBS score is the slope at the origin of this experimental variogram on a log-log representation. As it can be intuitively understood, a 3D image of a compact network at the trabecular level will produce 2D projection images with many grey-level variation of small amplitude and, therefore, a steep slope at the origin of the variogram and consequently a high value of the TBS variogram, using an algorithm adapted to the characteristics of the DXA images [3].
A low TBS value, in contrast, indicates a poor-quality architecture of the trabecular bone structure, with few grey-level variations of considerable amplitude, therefore a clement slope at the origin of the experimental variogram. As with BMD, the TBS values are calculated for each vertebra and for the overall region of interest. The values possessed by each pixel are shown in coded colours (green, yellow and red) on the final produced report, as shown in Figure 3.

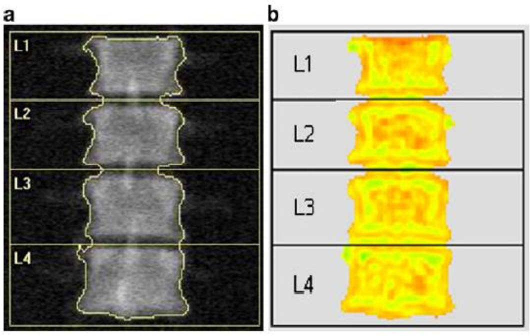


Figure 3: Application of TBS mask on DEXA bone segmentation

2.3 Bone Strain Index (BSI)

"Considerable effort has been done in order to define a patient-specific structural engineering and Finite Element Models (FEMs) of the proximal femur to estimate femoral strength and to assess hip fracture risk" [4].

Recently, it has been developed a bone FEM analysis on DXA images named Bone Strain Index (BSI), in order to take into account bone strength features in the prediction of a fracture risk. Bone Strain Index automatically calculates strains and stresses in a bone segment, starting from a specific loading condition, defined specifically for each patient. It is based on finite element algorithms usually used in engineering applications[4] The analysis performed by the Bone Strain Index can be applied both to the vertebral and femoral district.

3. Mini Health Technology Assessment (Mini-HTA)

Dual X-ray absorptiometry, nowadays, can be exploited by several image analysis methods to evaluate bone mass and density, bone microarchitecture and bone segments subjected to higher loadings. In 2016 it was installed GE-Bravo DEXA scanner in "Repubblica" site: the machine has been the gold standard technology for the diagnosis of skeletal pathological conditions. However, reasons related to the obsolescence of the machine with others related to the possibility to exploit useful innovation present at the state of the art, brought to the idea of the machine replacement. The aiming target of the technology was shaped with the users: for what concern the clinical part, the targeting technology was projected to perform normal DXA 2D image acquisitions at different skeletal sites, such as anteroposterior (AP) spine, dual femur and forearm. Moreover, the clinical requirement to be satisfied were about the introduction of innovative software for the execution of textural measurements, in order to acquire information not only about density quantity, but also regarding bone microarchitecture quality. For this way TBS integration was required, at least. The European network for Health Technology Assessment (EUnetHTA) is the preferred facilitator of high-quality HTA collaboration in Europe, that has the aim to connect public national/regional HTA agencies, research institutions and health ministers, enabling a standardized realization of HTA reports, based on fundamental criteria. Moreover, it supports an effective exchange of information to support policy decisions by Member States. [6]. At the beginning of 2016 it was released the HTA Core Model Version 3.0, that is a methodological framework for the production of such standardized HTA report. It's of our interest since a subgroup of the domains included in the Core Model was taken into account for the realization of this Mini-HTA report: in particular Description and technical characteristics of technology (TEC), Clinical effectiveness (EFF), Organizational aspects (ORG) and Costs and economic evaluation (ECO) domains were analyzed to order to produce indications for the final decision-making process.

Being already installed in "Via Larga" and "Nembro Esselunga" centres a Fujifilm brand DEXA, it has been convenient the consultation of an offer coming from this side. The model that was considered names FDX Visionary DR: its specifications were analyzed from the technical, clinical and structural point of view. The machine under analysis was equipped with a software algorithm called 3D-DXA, that assesses the proximal femur, only, from a standard hip DXA scan, providing to clinicians an advanced characterization of the cortical and trabecular structures.

Contacts have been established with Caresmed: their proposed model for the requirements presented was Lunar Prodigy PRO. In comparison with Fujifilm brand, that proposed a software inclusion based on the measurement of the cortical and trabecular density from a statistical shape and appearance model, GE brand included in the offering the Trabecular Bone Score (TBS) analysis, that instead provides as output an indication not on the trabecular density, but it allows to obtain an indication of the 3D distribution of the internal trabecular microstructure. The TBS software, after the acquisition of the vertebral DXA scan, will produce as output a report including a picture showing the normal DXA scan superimposed with a colorimetric mask indicating the zones more fracture-prone, going toward the red color, and fracture-resistant zones, going toward the green color.

The third and last proposal examined came from Technologic, one of the official distributors of Hologic technologies in Italy: the proposed model for the requirements presented was QDR Horizon Ci, a bone densitometer belonging to the last generation DXA scanners produced by Hologic. BMD, as mentioned in Section 2.1, can be defined as an evaluation of the bone quantity, TBS software, instead, permits to obtain an evaluation of the bone quality: with the objective to complete the clinical offer, Technologic company proposed another optional software tool named Bone Strain Index (BSI). The Bone Strain Index, as cited in Section 2.1, allows to obtain the strain distribution inside the scanned object, in order to get detailed information about geometry and load definition. Threshold values for the correct use of BMD, TBS and BSI measurements are provided in the following:

- Bone Mineral Density
    - *Normal.* T-score(BMD) ≥ -1.
    - *Low bone mass (osteopenia).* -1 > T-score(BMD) ≥ -2.5
    - *Osteoporosis*. T-score(BMD) < -2.5.
    - *Severe osteoporosis (established osteoporosis).* T-score(BMD) < -2.5 and in presence of one or more fragility fractures.
- Trabecular Bone Score
    - *Normal.* TBS > 1.31.
    - *Partially deteriorated trabecular structure.* 1.31 ≥ TBS > 1.23.
    - *Degraded trabecular structure.* TBS ≤ 1.23.
- Bone Strain Index
    - *Normal.* BSI ≤ 1.68.
    - *Partially reduced bone resistance.* 1.68 < BSI <.2.40.
    - *Reduced bone resistance.* BSI ≥ 2.40.

In endocrinology different case-studies can experience the improvement in the diagnostic capability of this instrumentation: it has been demonstrated that, except of osteoporosis, in which DEXA examination was established as a standard technology, many other pathologies, such as diabetes, PHPT, rheumatoid arthritis and more can benefit from the improvement in the facture risk assessment provided by the proposed software. The development of the clinical offer is, however, related to projects that are operationally feasible and economically sustainable. Therefore, a proper prior analysis of these conditions was performed.

4. Multi criteria decision analysis (MCDA)

Nowadays, Health Technology Assessment (HTA) is mainly conducted based on clinical effectiveness and safety studies and medico-economic studies. In addition, healthcare organizations are characterized by a high level of complexity and a very dynamic environment [7]: that's why multi-criteria decision analysis (MCDA) methods aim to facilitate the identification of the best possible solution to a given problem that requires considering a set of aspects or criteria, which are often heterogeneous. Core components of any MCDA method are:

- The alternatives in competition with one another.
- The criteria by which alternatives are assessed.
- The level of performance of each alternative for each criterion.
- The relative weight of each criterion.

A pseudo Best-Worst Scaling method was used for our purposes. The criteria included in the decision analysis were the ones taken into account for the production of the HTA report. In order to provide the same importance level to the domains under analysis, during the development of this phase it was decided to attribute equal weights to all the four domains. The most applied aggregation formula for combining the individual scores is the additive model, which is presented below:

$$V_j = \sum_{i=1}^{N} s_{ij} w_i$$

where V_j is the overall value of technology j, s_{ij} is the score for technology j on criterion i, and w_i is the weight attached to criterion i. A list containing specifications on each criterium that was taken into account for our purposes is presented below:

- *Clinical Effectiveness (EFF):*
  - Software packages included.
- *Description and technical characteristics of technology (TEC):*
  - Paediatric application.
  - Orthopaedic application.
  - Beam geometry.
  - DICOM 3.0 and HL7 compatibility.
- *Costs and economic evaluation (ECO):*
  - Price of the machine at first economic offer receipt.
  - Warranty period.
  - RX-tube replacement.
- *Organizational aspects (ORG):*
  - Technical Service response time, in case of technical issues.
  - Number of ordinary repairs in a year.
  - In stock availability of the target technology.

Starting from the EFF domain, it was considered as a first requirement the inclusion of a textural analysis, generated by a given software package, that was able to provide a description of the trabecular bone distribution as an indication of the bone quality, with respect only to a bone quantity description. Trabecular Bone Score (TBS) analysis, provides as output an indication not on the trabecular density, rather it allows to obtain an indication of the 3D distribution of the internal trabecular microstructure. Medimaps Group distributed TBS iNsight® to both the last two competitors (GE and Hologic), so there was no competition among the two participant on this side. However, the TBS technology cannot be applied to the femoral site since the trabecular distribution in the femur region is asymmetric and more complicated.[4] Hologic allowed to compensate for this restriction by introducing the Bone Strain Index; it allows to complete a diagnostic analysis on a body structure that is daily submitted to a given load since it permits to obtain a local strain distribution of the scanned object with the use of a FEA model. Moreover, instead of TBS technology, currently applied only on the lumbar spine site, BSI evaluation for the femoral region follows the same criteria used for the lumbar region. In terms of the technology characteristic (TEC), the last two competitors showed several differences. The paediatric module was included in both the technologies, but only Hologic provided for free also the orthopaedic application. For the ECO evaluation it was taken into account the purchasing price of the two technologies. A warranty period with a duration higher or equal than 12 months was considered as an acceptable threshold for assigning a score equal to one to this specific criterium. GE included in the contract a warranty period of 12 months, however Hologic proposed instead for two years of warranty period duration. For what concern the RX-tube replacement, General Electric included in the contract a single unit for free in case of damages, while Hologic proposed an unlimited number of units, during the warranty period. Therefore, also this further displacement was considered. For the ORG domain, the stock availability of the target technology has been a core theme to be analyzed in this evaluation. Not only, a Technical Service response time favored for Hologic, with eight hours of time window, with respect to GE, that presented for less than 24 hours of time window. This multi criteria evaluation allowed to attribute an overall value V_1 to GE group proposal equal to 2, while an overall value V_2 to Hologic proposal equal to 3.5. Therefore, the target solution was in this way identified as the Hologic proposal, with its Horizon Ci technology.

5. Operating Plan

A formal communication was sent to Technologic company: it was requested a schedule for the on-site installation, configuration and training of the technical personnel days. The Project Manager (PM) of Technologic provided a schedule of the working days divided into three sessions:

- Monday 04th July. The positioning of the technology in the installation site would have been followed by an internal engineer of Technologic company, who would have dedicated the rest of the working days for machine assembly and phantom calibration.
- Tuesday 05th July. Calibration complete, RIS/PACS connection and testing of the machine would have been performed.
- Wednesday 06th July. Training of technical personnel would have been performed during this current day.

6. Conclusions

The Department of Clinical Engineering allowed me for having this opportunity. This opening allowed me for the application of concepts and notions that were learnt during my personal path of study at Politecnico di Milano. Technical background in understanding the concepts related to imaging in diagnostics permitted to differentiate among the proposed alternatives with a rational comprehension, mostly related to the process to the generation of the image as first output of the DEXA scan. A particular interest with respect to the medical diagnostic field was provided firstly by personal experiences, and the subsequent confidence was then developed with the attendance to the academy. Not only, apart from the technical aspects, the skills that were needed to actualize this project from the managerial, operative and economic point of view were aspects that were never encountered before in my professional experience. Being the owner of a project means to have the responsibility to guide the entire workflow towards an effective, efficient and valuable management of subsequent tasks.

7. Bibliography

[1] H. Kröger, P. Vainio, J. Nieminen, and A. Kotaniemi, “Comparison of different models for interpreting bone mineral density measurements using DXA and MRI technology,” *Bone*, vol. 17, no. 2, pp. 157–159, Aug. 1995, doi: 10.1016/S8756-3282(95)00162-X.

[2] N. C. Harvey *et al.*, “Trabecular bone score (TBS) as a new complementary approach for osteoporosis evaluation in clinical practice,” *Bone*, vol. 78, pp. 216–224, Sep. 2015, doi: 10.1016/J.BONE.2015.05.016.

[3] V. Bousson, C. Bergot, B. Sutter, P. Levitz, and B. Cortet, “Trabecular bone score (TBS): Available knowledge, clinical relevance, and future prospects,” *Osteoporosis International*, vol. 23, no. 5, pp. 1489–1501, May 2012, doi: 10.1007/S00198-011-1824-6/FIGURES/5.

[4] F. M. Ulivieri and L. Rinaudo, “Beyond Bone Mineral Density: A New Dual X-Ray Absorptiometry Index of Bone Strength to Predict Fragility Fractures, the Bone Strain Index,” *Front Med (Lausanne)*, vol. 7, p. 1096, Jan. 2021, doi: 10.3389/FMED.2020.590139/BIBTEX.

[5] “Vision, Mission, and Values - EUnetHTA.” https://www.eunethta.eu/about-eunethta/mission-vision-and-values/ (accessed Oct. 25, 2022).

[6] A. Dubromel and M.-A. Duvinage-Vonesch, “Loïc Geffroy & Claude Dussart (2020) Organizational aspect in healthcare decision-making: a literature review,” *J Mark Access Health Policy*, vol. 8, no. 1, p. 1810905, 2020, doi: 10.1080/20016689.2020.1810905.