Calculation of Bone Mineral Density from Dual-energy CT and its Application on Patient with Multiple Myeloma

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Abstract—This article presents the results of the calculation of bone mineral density in the spine of a patient with multiple myeloma and lytic lesions. The findings indicate that the average value for a healthy vertebra falls within the physiological range. In the case of the patient with myeloma, a low value was measured in the area of the lytic lesion, suggesting a high risk of pathological fractures. The research also revealed lower values in areas without lytic lesions. These results emphasize the importance of precise evaluation of mineral density in the diagnosis of spinal diseases.

Index Terms—BMD, multiple myeloma, dual-energy CT, spine

I. INTRODUCTION

Multiple myeloma (MM) is a hematologic disorder marked by the clonal expansion of plasma cells within the bone marrow. It is commonly linked to skeletal issues, with osteolytic bone lesions serving as a key diagnostic indicator for disease progression and being incorporated into diagnostic criteria [1].

The main manifestations of MM are succinctly captured by the acronym CRAB, which represents hypercalcemia (C), renal impairment (R), anemia (A) and bone disease (B). Among these, bone disease emerges as the prevailing symptom, impacting more than 80 % of all patients [2], [3].

Identifying osteolytic lesions, a common manifestation of the condition, is crucial for implementing therapy immediately. In contemporary diagnostics, the integration of low-dose computed tomography (CT), along with magnetic resonance imaging (MRI) and hybrid imaging methods (particularly PET/CT), has become indispensable [4].

Dual-energy CT (DECT) is currently gaining prominence in the field of medical imaging. This technique involves the use of two different X-ray energies for imaging, allowing for energy decomposition and enhanced differentiation of signals. Unlike conventional CT (cCT) examinations, DECT enables the distinction between photons with different energy levels. Spectral CT (sCT) can also use multi-energy decomposition. Manufacturers employ different technical configurations, including two different X-ray energies or two-layer detectors with varying sensitivities to different X-ray energies, to achieve this capability. This functionality enables the utilization of post-processing software to generate multiple parametric maps, as well as what is known as virtual monoenergetic images (VMI) [5], [6].

The bone mineral density (BMD) plays a crucial role in assessing bone strength and resilience. This metric serves as a key indicator of bone integrity and can provide essential information on the risk of osteoporosis and fractures associated with bone weakening. Measurement of BMD is often performed using various diagnostic techniques, such as dual-energy X-ray absorptiometry (DXA) or Quantitative Computed Tomography (QCT). DXA, compared to other BMD estimation methods, has a low cost and low absorbed dose to the patient. However, DXA also has its disadvantages, such as the bias in values caused by the summation of soft tissue values with bone tissue. It is also a 2D imaging method, so the resulting area BMD estimate is the summation of the superficial cortical bone with the more metabolically active internal trabecular bone. Therefore, multi-energy X-ray computed tomography methods with three-dimensional output are used for a more detailed evaluation of mineral density distribution in trabecular bone. Most QCT methods are limited to the estimation of BMD of cortical and trabecular bone in the presence of a phantom without more extensive estimation of the partial volumes of the individual elemental components of trabecular bone; bone minerals, collagen, water, bone marrow, and fat components. The fat component reduces the CT number value, and collagen has the opposite effect. Therefore, it is reasonable to quantify the volumes of these components for proper calculation of BMD estimation [7].

Regarding the measurement by QCT, a BMD value between 80 and 120 mg/cm³ characterizes osteopenia, while a BMD value below 80 mg/cm³ defines osteoporosis [9]. Thus, these diseases can be diagnosed and distinguished based on BMD measurements.

This paper focuses on initial experiments to calculate and analyze BMD utilization in a database of 10 patients, 5 with confirmed MM and 5 without spinal pathology.
II. MATERIALS AND DATA

In this study, an anonymized database of ten patients was utilized, consisting of five oncological cases with multiple myeloma presenting lytic lesions in the spine, and five patients with spine images showing a pathological-free condition. Data were acquired with the approval of the ethics committee under the application registration number NU23J-08-00027, and all patients provided informed consent. The information was obtained through Philips Healthcare IQon spectral CT in collaboration with the University Hospital Brno, Department of Radiology and Nuclear Medicine.

The scanning acquisition parameters included a peak tube voltage of 100 kV, tube current of 10 mA, matrix size of 512 × 512, and slice thickness of 0.9 mm using a sharp reconstruction kernel and hybrid iterative reconstruction technique (iDose4, set to level 4). Scans covered from the head to the knees with the upper limbs crossed over the abdomen. Finally, the scans were reviewed using a specialized workstation (Intellispace Portal version 12.1; Philips Healthcare) by two independent readers. The diagnosis of multiple myeloma was established based on elevated levels of monoclonal immunoglobulin in the blood and an increased count of plasma cells in the bone marrow. Spectral CT with a low-dose protocol was performed for the initial staging of the disease, following recommendations of the International Myeloma Working Group (IMWG).

Raw SBI format spectral CT data were available for each patient. Spectral CT enabled reconstruction of various parametric images including conventional CT, virtual monoenergetic images at different energies, calcium suppression images, and others using a dedicated workstation (Intellispace Portal version 12.1; Philips Healthcare).

For the purpose of this paper, conventional CT images and virtual monoenergetic images at 40, 80, and 120 keV were reconstructed and used. An example of the available data is shown in Fig. 1.

For the calculation of BMD in this paper, the methodology presented in [10] was used. The mass attenuation coefficient for an absorber comprising a blend of elements can be determined through the following formula:

$$\left( \frac{\mu}{\rho} \right)_T = \sum_{i=1}^{N} \left( \frac{\mu}{\rho} \right)_i \cdot W_j$$  \hspace{1cm} (1)

where \( \left( \frac{\mu}{\rho} \right)_i \) is the mass attenuation coefficient of individual elements at photon energy \( i \), \( W_j \) represents the fractional weight of each element, \( \mu \) represents the attenuation coefficient, \( \rho \) represents the mass density, \( N \) represents the number of elements, and \( \left( \frac{\mu}{\rho} \right)_T \) represents the total mass attenuation coefficient.

With the use of this relationship and the standard photon-attenuation tables for the elements, the mass and linear attenuation coefficients for any substance can be determined. The trabecular part of a vertebra consists mainly of five distinct materials: bone mineral, collagen matrix, water, red marrow, and adipose tissue. The mineral content within the bone consists primarily of poorly crystallized calcium hydroxyapatite \( Ca_{10}(PO_4)_{6}(OH)_2 \), distributed throughout the collagen matrix.

The mass attenuation coefficients of the components found in trabecular bone are connected to the measured CT numbers in Hounsfield units through the following equation:

$$CT \ number = K \left[ \sum_{i=1}^{N} \left( \frac{\mu}{\rho} \right)_i \rho_i \right] - 1$$  \hspace{1cm} (2)

where \( K \) is a constant, approximately equal to 1000 for most CT scanners. This relationship can be reformulated as follows:

$$CT \ number = \alpha \rho_{BM} + \eta \rho_C + \omega \rho_W + \beta \rho_F + \theta \rho_M + \delta + \epsilon$$  \hspace{1cm} (3)
where $\alpha$ (calcium hydroxyapatite), $\eta$ (collagen), $\omega$ (water), $\beta$ (adipose tissue), and $\theta$ (red marrow) are attenuation coefficients dependent on photon energy, $\delta = -1000$ HU, $\epsilon$ is the number of offset of water, and $\rho_{BM}$, $\rho_C$, $\rho_W$, $\rho_F$, and $\rho_M$ are concentrations of bone mineral, collagen matrix, water, adipose tissue, and red marrow, respectively, in grams per cubic centimeter (g/cm$^3$).

The equation that connects measured CT numbers to concentrations of different substances in the cancellous bone of the spine can be simplified by considering its structure. The trabecular compartment is intricately woven with a complex network of collagen matrix that houses the bone mineral. The collagen matrix has minimal water content in older individuals, who are the most common subjects for bone mineral measurement. The remaining space surrounding the collagen matrix is mainly occupied by red marrow and adipose tissue in various proportions. The water in this part of the trabecular space is sufficiently similar in density and photon-attenuation properties to that in the red marrow, allowing them to be combined as non-adipose tissue ($\rho_T$), as expressed in the following equation:

\[ \omega \rho_W + \theta \rho_M = \gamma (\rho_W + \rho_M) \equiv \gamma \rho_T \quad (4) \]

Moreover, the ratio of bone minerals to collagen in the matrix remains relatively consistent in the majority of elderly individuals. Decalcified matrix is only found in specific cases (e.g., osteomalacia). On the contrary, osteoporosis leads to an individual. Decalcified matrix is only found in specific cases (e.g., osteomalacia). On the contrary, osteoporosis leads to an individual. The density of collagen ($\omega$) is approximately 1.92 g/cm$^3$ in older individuals. The density of collagen $C$ alone is 1.38 g/cm$^3$, and the density of bone mineral ($l$) alone is 3.06 g/cm$^3$. Therefore, the expression can be written as follows:

\[ \rho_{TB} = \frac{lV_{BM} + CV_c}{CV_{BM} + V_c} \quad (5) \]

where $V_{BM}$ and $V_c$ are volumes occupied by bone mineral and collagen, respectively, per cubic centimeter. This equation can be rewritten as follows:

\[ V_c = \frac{(l - \rho_{TB})V_{BM}}{(\rho_{TB} - C)} = \lambda V_{BM} \quad (6) \]

where

\[ \lambda = \frac{l - \rho_{TB}}{\rho_{TB} - C} \quad (7) \]

In addition, the total volume ($V_{TB}$) occupied by the matrix material (bone mineral plus collagen) must be equal to the sum of its parts, which can be expressed as follows:

\[ V_{TB} = V_{BM} + V_c = V_{BM} + \lambda V_{BM} \quad (8) \]

and

\[ V_c = \frac{\lambda V_{TB}}{1 + \lambda} \quad (9) \]

The densities of collagen and bone minerals in trabecular bone tissue are known, as are the densities of fat-free tissue and adipose tissue. The value of the density of fat-free tissue, typically denoted $g$, is reported as 1.02 g/cm$^3$, and the density of adipose tissue, denoted $t$, is 0.92 g/cm$^3$ [11]. These densities can be expressed as $\rho_T = gV_T$ and $\rho_F = tV_F$, where $V_T$ and $V_F$ are the volumes of fat-free tissue and adipose tissue, respectively.

When using modified partial equations and relationships from (3), the number of unknown variables is reduced to three partial volumes of bone minerals and collagen ($V_{TB}$) and volumes of tissue with fat ($V_F$) and without fat ($V_T$). Since the total volume must be equal to 1 cm$^3$, (3) simplifies to two unknown variables: $V_T = 1 - V_{TB} - V_F$. The relationship of the CT number to the fractional volumes reduces to the following equation:

\[ \text{CT number} = \mu V_T + \beta tV_F + \gamma g(1 - V_{TB} - V_F) + \delta + \epsilon \quad (10) \]

where

\[ \mu = \frac{\alpha l + \eta C l}{1 + \lambda} \quad (11) \]

Equation (10), involving two unknowns $V_F$ and $V_{TB}$, can then be easily solved as a system of two equations using X-ray radiation with two distinct energies in a dual-energy CT system:

\[ \text{CT number} = (\mu - \gamma g)V_{TB} + (\beta t - \gamma g)V_F + \gamma g + \delta + \epsilon \quad (12) \]

and

\[ \text{CT number}' = (\mu' - \gamma g)V_{TB} + (\beta' t - \gamma g)V_F + \gamma' g + \delta + \epsilon' \quad (13) \]

Where (12) is the equation for higher energy radiation, and (13) is the equation for lower energy radiation. From the values of $V_{TB}$ and $V_F$, many other variables that are of interest to the clinician can be determined, as follows: $V_T = 1 - V_{TB} - V_F$ is non-adipose fractional volume per cubic centimeter, and

\[ \rho_{BM} = \frac{l + V_{TB}}{1 + \lambda} \quad (14) \]

where (14) expresses the density of bone mineral (BMD) in g/cm$^3$.

The total density of the trabecular bone in the vertebral body, in g/cm$^3$, can be calculated as follows:

\[ \rho_{TBV} = \rho_{BM} + C\lambda V_{TB} + tV_F + gV_T \quad (15) \]

The density of hydroxyapatite ($\rho_{BM}$) is represented by calcium, accounting for 39.9%; $\rho_{Ca} = 0.399\rho_{BM}$. 

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IV. RESULTS AND DISCUSSIONS

This initial study used virtual monoenergetic images at 80 and 120 keV to estimate BMD. BMD and other substances were calculated only in the spine region using the available spine segmentation mask. An example of the available data in the conventional CT bone radiology window, along with a VMI at 40 keV and the calculated BMD map for the vertebra of a patient with multiple myeloma and a marked lytic lesion and region of interest (ROI) of trabecular tissue, can be seen in Fig. 3. On the contrary, Fig. 4 presents an example of the same images for the vertebra of a patient without spinal pathology. It can be seen from the images that the contrast between the lesion and the surrounding tissue is much better on the 40 keV VMI than on conventional CT. Even better contrast is evident on the BMD map, where the resulting image is also much smoother.

To evaluate the differences in calculated BMD values between healthy vertebrae and vertebrae affected by lytic lesions, ROIs of trabecular tissue of lumbar vertebrae L1, L2, and L3 of the same patient with multiple myeloma were selected for demonstration, where vertebra L1 was affected by a lytic lesion marked by a radiologist. Furthermore, the L1 and L2 vertebrae of the patient without pathology in the spine were selected. Box-and-whisker plots were created from ROIs of conventional CT data (see Fig. 5) and from the BMD map (see Fig. 6). The examples clearly illustrate that the disparity between the lytic lesion, the vertebrae of the patient with multiple myeloma, and those of the healthy spine is significantly greater on the BMD map compared to conventional CT.

From the ROIs, the mean value and standard deviation were calculated. Tab. I showing mean values (with standard deviations) extracted from ROIs on conventional CT, VMI at 40 keV, and BMD map. MM denotes a patient with multiple myeloma, while H denotes a healthy patient. ROI refers to regions of interest derived from trabecular tissue.

Based on the results obtained and references to the literature, it can be concluded that the calculated BMD results are in line with expectations. The mean BMD values of 222 and 217 g/cm$^3$ for healthy vertebrae fall within the physiological
Fig. 5. The box-and-whisker plot displays ROIs from conventional CT. The lytic lesion is highlighted in red, ROIs from the patient with multiple myeloma are in purple, and ROIs from healthy vertebrae are in green.

Fig. 6. The box-and-whisker plot displays ROIs from BMD map. The lytic lesion is highlighted in red, ROIs from the patient with multiple myeloma are in purple, and ROIs from healthy vertebrae are in green.

range for healthy tissue. On the contrary, in a patient (female, 66 years) with multiple myeloma and lytic lesions in the spine, a mean BMD value of 62 g/cm³ for lytic lesions indicates a high risk of pathological fractures at this site. Regarding the ROI of the same vertebra, the calculated mean BMD value of 152 g/cm³ suggests a moderate impact of osteoporosis on the rest of the vertebra. When examining other vertebrae from the same patient without lytic lesions, the mean BMD values of 132 and 156 g/cm³ suggest that although there are no significant lytic lesions, the vertebrae exhibit lower BMD values than would be physiological. This could be due to factors such as patient age, diffuse MM infiltration, or incipient osteopenia/osteoporosis.

V. CONCLUSION

This article presents the results of the calculation of bone mineral density (BMD) in the vertebrae of a patient with multiple myeloma and lytic lesions in the spine. The findings indicate that the average BMD value for a healthy vertebra falls within the physiological range. In the case of the patient with myeloma, a low BMD value was measured in the area of the lytic lesion, suggesting a high risk of pathological fractures. The research also revealed that BMD was lower than physiological even in areas without lytic lesions. The results are promising for future research, indicating that BMD maps could serve as valuable parametric input maps for segmenting lytic lesions in the spine and for further analysis.

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REFERENCES


### TABLE I

**AVERAGE VALUES AND STANDARD DEVIATIONS OF THE ROIs**

<table>
<thead>
<tr>
<th>Region of interest</th>
<th>Conv CT [HU]</th>
<th>VMI [HU]</th>
<th>BMD [g/cm³]</th>
</tr>
</thead>
<tbody>
<tr>
<td>MM - L1 - lesion</td>
<td>84 (38)</td>
<td>160 (56)</td>
<td>62 (17)</td>
</tr>
<tr>
<td>MM - L1 - ROI</td>
<td>166 (35)</td>
<td>398 (81)</td>
<td>152 (25)</td>
</tr>
<tr>
<td>MM - L2 - ROI</td>
<td>149 (60)</td>
<td>401 (110)</td>
<td>156 (36)</td>
</tr>
<tr>
<td>MM - L3 - ROI</td>
<td>140 (46)</td>
<td>341 (83)</td>
<td>132 (28)</td>
</tr>
<tr>
<td>H - L1 - ROI</td>
<td>278 (32)</td>
<td>622 (42)</td>
<td>222 (13)</td>
</tr>
<tr>
<td>H - L2 - ROI</td>
<td>270 (35)</td>
<td>604 (54)</td>
<td>217 (17)</td>
</tr>
</tbody>
</table>