RESEARCH PROTOCOL

Developing a Bone Mineral Density Distribution Model to Reduce the Risk for Postoperative Hip Surgery Complications in Racial Minorities: A Research Protocol

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Abstract

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Introduction: Racial minorities, including Black and Hispanic populations, suffer more postoperative hip surgery complications relating to fixations and replacements than White populations. The goal is to use CT scans and 3D projections to create a bone mineral density distribution model for these racial groups.

Methods: A preliminary trial of the proposed methods was conducted to ensure reliable data could be obtained. Semiautomatic segmentation of left femurs from decedents was done in 3D Slicer, followed by mean bone mineral density analysis.

Discussion: Preliminary trials show that the BMD processing pipeline gives viable results for sample groups of 5 CT scans. Future studies done with this research protocol will involve a larger sample size and the inclusion of machine learning extensions that will reduce the processing time of the CT scans. Confounding variables not considered in the preliminary trial will also be analyzed.

Conclusion: The use of the streamlined pipeline in conjunction with other imaging software could provide an alternative to bone mineral density imaging, as well as lead to the development of models for minorities with less representation in medical data.

Keywords: bone mineral density; racial groups; computed tomography; 3D modelling; femur; hip surgery

Introduction

Hip injuries are one of the most common ailments affecting middle-aged and elderly populations in the developing world. These include, but are not limited to, hip fractures. Currently, individuals 50 years of age and older are most susceptible to hip fractures, with the risk being higher for women at 20%, compared to 5.6% for men [1]. These numbers are further increased by pre-existing medical conditions, such as osteoporosis [1]. It has been estimated that the incidence of hip fractures will reach 2.6 million cases worldwide by 2025 and nearly double to 4.5 million in 2050 [1].

Hip arthroplasties with prosthetic implants are used in cases of serious hip injury in which the bone cannot reliably heal due to damage or lack of regenerative ability, such as in cases of osteoarthritis [2].

Natural bone thinning, known as osteolysis, may cause loosening of hip implants over time and this risk is increased if the patient has a low bone mineral density when the surgery is first performed [2,3]. Internal fixation, which is a common method used to stabilize fractures, can have a high failure rate in thinning bone. It has been shown that implant construct failures can occur due to variations in bone density in both the cortical and trabecular bone [4]. Studies have shown that up to 10-25% of internal fixations

Xi et al. | URNCST Journal (2022): Volume 6, Issue 10 DOI Link: <u>https://doi.org/10.26685/urncst.397</u> using screws and plates result in failure due to the bone being unable to support the devices [4]. Previous research has shown that a decrease in bone mineral density (BMD) can be an indicator of thinning bone and possible success of hip fixations and implants [4].

Racial Discrepancies

Racial minorities tend to have worse prognoses and surgical outcomes, including higher risk for blood clots and postoperative infections, compared to white populations [5]. In one study, Black patients were found to be more than 30% less likely to undergo total knee or hip replacement compared to white patients, despite both racial groups being equally as likely to experience advanced arthritis [6]. Due to minorities being less likely to seek treatment, data available for hip surgeries leans in favour of middle-aged and elderly white patients [5,6].

Medical Imaging vs. Other Methods for Determining BMD

Although the presence of minerals, such as serum 25-hydroxyvitamin D (25(OH)D), in blood plasma can indicate bone density levels, this may not be an accurate measure. Studies have shown that Black and Hispanic populations have lower internal concentrations of 25(OH)D compared to white populations, despite having sturdier

bone structure and higher BMD in the femur, especially the femoral neck area [3,7,8]. Therefore, medical imaging may be a more reliable and less invasive method to determine bone density compared to serum 25(OH)D measurements and other biopsy procedures [8].

This research protocol devises a method to determine differences between bone density distribution of Black, Hispanic, and White populations. This data will be used in conjunction with BMD distribution mapping for the potential development of generalized BMD models for minorities, which can be used as guides for implant designs which are less likely to cause postoperative complications. The protocol aims to determine whether a reliable BMD model among different races can be produced using computed tomography (CT) scans and 3D imaging software. The model will eventually be used to determine if there are any significant differences in BMD between races. CT scans were chosen due to their abundance in medical protocol and their relative inexpensiveness compared to other scanning modalities. Existing scan types such as dualenergy x-ray absorptiometry (DEXA) can differentiate bone density by subtracting the soft tissue from the resulting xray image, allowing bone density to be analyzed independently [8]. However, DEXA scans are limited to two dimensions and are difficult to access due to higher costs compared to CT scans [8].

Methods

A preliminary test of the methodology was conducted with a small sample size to determine if reliable data could be obtained with the proposed methods.

Decedents

Black, White, and Hispanic populations were chosen as the sample groups, due to the abundance of data for those groups in the New Mexico Decedent Image Database (NMDID) [9], from which the CT scans in Digital Imaging and Communications in Medicine (DICOM) format were downloaded. These were scanned using NMDID's Adult OMI Protocol [9], whose scanner settings include a 120 kilovoltage peak (kVp), matching the settings of the Hounsfield Unit (HU) to BMD conversion adapted from Schwaiger et. al. [10] Hounsfield units are an arbitrary scale used to measure the intensity of CT scans [10].

All decedents died from natural causes, mainly cardiac arrhythmia, but also from obstructive pulmonary lung disease and hypertension. The scans were selected from the database using a filter of Black or African American, Hispanic, and White decedents for race. The age range of 50-90 was chosen due to the tendency for hip ailments and injuries to occur at this age in adults [1].

A sample of 5 male and 5 female CT scans for each race were analyzed, for a total of 30 scans. Due to study limitations, confounding variables such as living weight, drug use, and previous medical conditions were not considered in the preliminary trial. The six groups were

Xi et al. | URNCST Journal (2022): Volume 6, Issue 10 DOI Link: <u>https://doi.org/10.26685/urncst.397</u> Hispanic Males, Hispanic Females, White Males, White Females, Black Males, and Black Females.



Figure 1. Segmentation pipelines used for preliminary data collection. Flowchart created using LucidChart.com. Head, Neck, and GT shown in Blue, Yellow, and Red, respectively. Images obtained from NMDID and 3D Slicer [9,11].

Data Collection

Bone Torso CT scan files in DICOM format was downloaded from NMDID and loaded into 3D Slicer [11]. The volume was cropped to show only the left femur head and shaft at the proximal end. The femur was semiautomatically segmented in 3D Slicer, first using the threshold masking tool such that as much cortical and trabecular bone was included as possible. This was followed by painting the femur and pelvis bones as separate segments every 3-4 slices, then using the "Grow from Seeds" and "Wrap Solidify" [12] functions to segment as much of the femur as possible. "Erase" and "Smoothing" functions were used to remove stray grains of segmentation from the 3D model [13-19].

The segment was split into Head, Neck, and Greater Trochanter (GT) regions. These three regions were chosen due to the neck being one of the most studied areas of the femur with regards to bone density in previous studies[8], and the head and GT were chosen for being close to the neck and for being at risk for hip injuries [8]. Using 3D Slicer's "Statistics" module, the mean and standard deviation HU values were obtained for each group of scans, separated into femur head, neck, and greater trochanter in an output table [13,14,15,16,17,18,19].

3D Shape and BMD Modelling Using Bonemat

Bonemat is an open-source software that allows for DICOM HU values to be mapped onto a femur mesh provided by the user [20]. The following steps will be done to femur segmentations before processing in Bonemat:

- Export 3D segmentation of femur in .stl file format from 3D Slicer
- Smooth mesh to remove ridges and holes
- Convert mesh into finite element mesh

The DICOM files from the CT scans are needed to project the scan's HU values onto the mesh baseline in Bonemat, as shown in Figure 2. This resulted in the bone density being mapped based on HU values, which gave a rough distribution pattern. Bonemat does not give density values, therefore, the data needs to be paired with mean density values from 3D Slicer [11,20].



Figure 2. BMD distribution of a sample femur from a White Male, imaged using Bonemat [20]. Dark blue represents the least dense areas; red represents the densest areas.

HU to BMD Conversion

The Schwaiger study obtained the HU to BMD calculation using a combination of quantitative CT and multidetector CT, one of which used 120 kVp settings, which matches the settings used for NMDID's Adult OMI

Xi et al. | URNCST Journal (2022): Volume 6, Issue 10 DOI Link: <u>https://doi.org/10.26685/urncst.397</u> Protocol [10]. HU values from 3D Slicer were converted to BMD using the equation adapted from Schwaiger et. al [10]:

BMD = HU * 0.78

BMD was measured in mg/cc (milligrams per centimetre cubed). The study conducted by Schwaiger et. al involved lumbar vertebrae instead of femurs [10]; the assumption was made that BMD processing would be the same for both areas.

Preliminary Results

Figure 3 shows the distribution of bone density in the Head, Neck, and GT for the six sample groups. Given the small sample sizes for each group, no final conclusions regarding BMD in relation to race and sex can be reliably made from this data; however, the mean BMD appears to show a larger range across the GT for all three races, which may suggest that BMD is highly variable in the GT. BMD range for the femoral neck also appears to be more compact, which is consistent with previous findings [7]; however, the mean BMD in the neck for the Black sample groups was lower than both Hispanic and White groups. Further data collection is required to obtain more reliable conclusions for these sample groups, but the preliminary results show promise as they illustrate some differences in BMD across the races and sexes analyzed.

Anticipated Results for Future Research

Based on our preliminary results and findings of previous studies, we expect the mean neck BMD to remain compact, and the mean GT BMD to have the largest IQR out of the three analyzed femur sections. The Bonemat distribution imaging is expected to display higher BMD in the neck area, and to be variable in the GT area for all sample groups. The preliminary results for mean BMD in the head should remain constant for all three races in the female groups, whereas the mean head BMD for males appears to encompass a large range for Black males.

Discussion

The preliminary results were obtained to determine if the 3D Slicer pipeline produced reasonable results when converting from HU to BMD. Figure 3 shows that the BMD ranges fall within recorded values for BMD in adults [7].

However, the sample size used in preliminary data collection does not reflect general populations for several reasons, including a small sample size (30) and confounding variables such as drug use and living weight, which were not considered in the preliminary study. The scans were decedents that were all residents of New Mexico, USA, which does not encompass the general population who would benefit from bone mineral density models.



Figure 3. Mean BMD in the Femoral Head, Neck, and GT for Hispanic, Black, and White Males and Females. Circular points indicate an outlier (falls outside \pm 1.5 IQR). Box-and-Whisker plots created with RStudio [21].

Additional Data Processing

The preliminary results indicate that there are possible differences in BMD among different races, and with a larger sample size (20+ samples per group), the following statistical inferential methods can be used to evaluate and analyze the results: hypothesis testing alongside difference of mean confidence intervals, and linear regression models.

95% and 99% intervals are the most used difference of mean intervals in practice. In an extension to this research protocol, these could be used to confirm differences between the mean bone densities of the different races at a certain confidence interval. If bone density does not differ significantly, 0 would be inside our confidence interval, otherwise, 0 falls outside the confidence interval. This information would give insight as to whether current medical practices need adjustments when treating patients from different races.

Simple linear regression models could be used to showcase correlation between previously confounding variables, such as Age of Death and Living Weight. A scatterplot of the data, the correlation coefficient or the covariance, and confidence intervals would be used to determine a trend and deduce evidence of a relationship between the variables. This information could be useful to determine limitations to the data. For instance, if a strongly negative correlation between BMD and Age of Death can be seen, then this would be considered a limitation of the data set.

Software Extensions

Segmentation was completed manually as it allowed for greater segment accuracy and did not incur major time losses due to the small sample size. Potential use of an Artificial Intelligence-assisted segmentation module in 3D Slicer will be investigated in future endeavours that use larger sample sizes.

Another semi-automatic method for segmentation may be used instead. In this method, all CT scans of a group (Black Females, White Males, etc.) are non-rigidly registered onto each other using the Elastix module available in 3D Slicer [11]. This was to ensure that the different regions of the femur could be split evenly among the femurs, as well as to ensure consistency among average HU values. This method may be less accurate due to image warping from registration, but less time consuming.

Schwaiger et. al calculated prediction errors of 13.5 mg/cc root-mean-square error [10], which was not considered in the preliminary trial, but would need to be considered in future studies with a larger sample size, if the same HU to BMD equation were still to be used.

Using CT scans to image BMD distribution would provide an alternative method to DEXA that is less expensive and more accessible to disadvantaged minorities. Additionally, more information on bone density variance among minorities would allow for greater customizations to hip fixation implants and total hip replacements, thus resulting in more desirable postoperative outcomes. Largescale data could potentially be used to design devices with less chance of loosening or causing long-term impacts.

Work in the next 1-2 years will focus on data from the NMDID, with possible extensions into other decedent databases. Data collection from living participants will also be considered if the required ethics approval is obtained

The preliminary trials using the data collected with 3D Slicer and analysis in RStudio provide a promising approach to developing a BMD Distribution modelling pipeline that is only dependent on CT scans. Although DEXA scans may provide more accurate results, the increased radiation exposure and cost that comes with DEXA scans may be enough to justify the use of a CT scan pipeline instead.

Conclusions

This research protocol aims to outline a method to produce BMD distribution models on the femur for Black, White, and Hispanic populations using 3D segmentation and HU mesh projection. The protocol involves obtaining the mean BMD values of three different femur sections the head, neck, and GT - using semi-automated segmentation in 3D Slicer. This will be followed by the projection of CT scans onto a finite element mesh to display BMD distribution across the femur.

Early results show that the proposed 3D Slicer and Bonemat pipeline appears to be promising as it gives viable results for BMD that fall within the range of calculated BMD for adults. With further testing of the model using a larger sample of 60-120 scans in total, more definite conclusions can be drawn regarding mean BMD and distribution for a population group.

Using CT scans as input provides a safer and more inexpensive method to image BMD compared to existing methods such as DEXA, which involve a higher radiation dosage. Although planned research will involve using decedent images, potential use of the BMD model with living patients may lead to lower risk for postoperative complications as patient BMD distribution can be used to create custom fixation and implant apparatuses based on distribution patterns.

List of Abbreviations Used

BMD: bone mineral density CT: computed tomography 25(OH)D: 25-hydroxyvitamin D DEXA: dual-energy x-ray absorptiometry NMDID: new mexico decedent image database DICOM: digital imaging and communications in medicine

Xi et al. | URNCST Journal (2022): Volume 6, Issue 10 DOI Link: <u>https://doi.org/10.26685/urncst.397</u> kVp: kilovoltage peak HU: hounsfield unit GT: greater trochanter

Conflicts of Interest

The authors declare that they have no conflict of interests.

Ethics Approval and/or Participant Consent

No ethical approval is required to make use of publicly available and anonymized NMDID data.

Authors' Contributions

JJYX: contributed to the study's design, collected, and analyzed data, drafted and revised the manuscript, and gave final approval of the version to be published.

CKE: contributed to the study's design, collected, and analyzed data, drafted and revised the manuscript, and gave final approval of the version to be published.

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