**MRI-based synthetic CT of the hip: can it be an alternative to conventional CT in the evaluation of osseous morphology?**

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**Abstract**

**Objectives**: MRI is the gold standard for soft tissue evaluation in the hip joint. However, CT is superior to MRI in providing clear visualization of bony morphology. The aim of this study istotest the equivalency of MRI-based synthetic CT to conventional CT in quantitatively assessing bony morphology of the hip.

**Materials and Methods**: A prospective study was performed. Adult patients who underwent MRI and CT of the hips were included. Synthetic CT images were generated from MRI using a deep learning-based image synthesis method. Two readers independently performed clinically relevant measurements for hip morphology, including anterior and posterior acetabular sector angle, acetabular version angle, joint space width, lateral center-edge angle, sharp angle, alpha angle and femoral head-neck offset on synthetic CT and CT. Inter-method, inter-reader, intra-reader reliability and agreement was assessed using calculations of intraclass correlation coefficient, standard error of measurement and smallest detectable change. The equivalency among CT and synthetic CT was evaluated using equivalency statistical testing.

**Results**: Fifty four hips from twenty seven participants were included. There was no reported hip pathology in the subjects. The observed agreement based on reliability and agreement parameters indicated a strong degree of concordance between CT and synthetic CT. Equivalence statistical testing showed that all synthetic CT measurements are equivalent to the CT measurements at the considered margins.

**Conclusion**: In healthy individuals we demonstrated equivalency of MRI-based synthetic CT to conventional CT for the quantitative evaluation of osseous hip morphology, thus obviating the radiation exposure of a pelvic CT examination.

**Key words (MESH):**

Tomography, X-ray Computed, Magnetic Resonance Imaging, deep learning, femur head, acetabulum

**Key points**:

MRI-based synthetic CT images can be generated from MRI using a deep learning-based image synthesis method.

MRI-based synthetic CT is equivalent to CT in the quantitative assessment of bony hip morphology in healthy individuals.

MRI-based synthetic CT is promising for use in preoperative diagnosis and surgery planning.

**Abbreviations**: 3DT1MGE=3 dimensional T1-weighted radio-frequency-spoiled multiple gradient echo, sCT= synthetic CT, ICC= intraclass correlation coefficient, SEM= standard error of measurement, SDC= smallest detectable change, AASA= anterior acetabular sector angle, PASA= posterior acetabular sector angle, SA= sharp angle, LCEA= lateral center-edge angle, AVA= acetabular version angle, JSW= joint space width, AA= alpha angle, FO= femoral offset.

**Introduction**

For diagnosis and pre-operative evaluation of hip dysplasia and femoroacetabular impingement, radiographs, CT, and MR imaging of the hip are frequently obtained [1]. Radiography is the modality of choice for screening purposes, while CT is most often used for surgical planning and more detailed assessment of osseous morphology [2, 3]. Preoperative CT has also been shown to improve surgical results [4, 5]. However, CT without intra-articular contrast does not offer great visualization of the labrum and cartilage thus MRI is often ordered in conjunction with CT for soft tissue evaluation [6]. In addition, most of the patients who are affected by these pathologies are young [7], so the CT radiation dose to the pelvis should be kept to a minimum.

Therefore, it would be useful to generate synthetic CT (sCT) data demonstrating bony anatomy from MRI. A novel MR technique for sCT generation has been developed, using a deep learning based postprocessing tool that accurately transforms gradient echo (GRE) derived MRI properties of tissues to Hounsfield Units (HU) [8]. Previous studies assessed osseous hip morphology with MRI techniques facilitating osseous structure visualization, including gradient echo (GRE) MRI [9, 10, 11], ultrashort echo time (UTE) [12] and zero echo time (ZTE) MRI [13]. GRE MRI is subject to artifacts and lacks reliability for cortical and subcortical bone. Limitations of ZTE-MRI and UTE-MRI include the limited availability, the requirement of high-end gradients and scanner hardware, the need for dedicated image processing, the shortage of specificity for cortical bone and the lack of quantitative HU maps [14]. In contrast, the deep learning-based sCT was developed for visualizing osseous structures by providing quantitative HU maps [15]. The postprocessing of sCT images is a fully automatic process that obviates the requirement for time-consuming manual postprocessing by trained operators and the algorithm uses a GRE pulse sequence that may be run on multiple vendor platforms [15] without specialized technical requirements (e.g. coil, gradient, and pulse sequence technology).

The purpose of this study isto test the equivalency of MRI-based sCT to conventional CT in quantitatively assessing bony morphology of the hip.

**Materials and Methods**

For this prospective study written informed consent was provided by all participants. Approval was obtained from the local medical ethical committee. Authors without conflicts of interest had full control of inclusion of any data and information submitted for publication.

Study Participants

Patients with inflammatory type low back pain suspected for having inflammatory sacroiliitis were referred by the rheumatologists at the outpatient clinic for pelvic MRI and agreed to undergo a CT on the same day. From February 2019 to November 2020 these patients were included in the present analysis. Pregnant patients, patients with metal implants in the pelvis or any contraindications to MRI were excluded.

CT protocol

Participants underwent a CT scan (Somatom Definition FLASH, Siemens Healthineers, Erlangen, Germany) using a dual-energy CT protocol: collimation: 32 × 0.6 mm; pitch: 0.6; rotation time: 0.5 second; tube voltages: 140 kV and 100 kV; kernel: 150F medium sharp; iterative reconstruction Safire; no tin-filter; no administration of intravenous contrast

MRI protocol

For sCT generation MR images were obtained on a 3.0 T MRI unit (Prisma, Siemens Healthineers, Erlangen, Germany) using an axial 3 dimensional T1-weighted radio-frequency-spoiled multiple gradient echo (3DT1MGE) sequence: 2 echoes: repetition time/echo time 1/echo time 2: 7/2/3.5 ms, field of view: 400×400 mm, acquisition matrix: 384×384, voxel size: 0.52 × 0.52 × 0.8 mm, acquisition time: 5 minutes 37 seconds. In addition, routine coronal T1-weighted turbo spin echo imaging, coronal short tau inversion recovery (STIR) imaging and axial STIR imaging sequences were performed.

Synthetic CT reconstruction

SCT images were reconstructed with the BoneMRI Pelvic region software (version 1.2, MRIguidance). The software reconstructed sCT images from two 3DT1MGE images derived from two different echoes using a deep learning method based on the U-net architecture [8]. This method exploits local spatial contextual information in the multi-echo data to reconstruct the latent bone structures, which was learned using paired MRI and CT data. MRI-derived tissue properties include combinations of in-phase, opposed-phase, fat-only, water-only, and water-fat decomposition images [8]. The software runs on site and is connected to the hospital picture archiving and communication system (PACS). The sCT images were generated without manual inputs through an automated pipeline facilitating a fully automated MRI-to–PACS processing time of 30 minutes. In this study, this was performed using a Horos PACS (version 3.3.5, Nimble Co. LLC).

Image analysis

On each scan two hip joints were analysed. SCT and CT images were reconstructed in the axial, coronal and axial oblique femoral plane for each joint, with a slice thickness and increment of 1 mm. Two radiologists (L.M., M.C., with 8 and 5 years of experience respectively) independently performed clinically relevant angular and distance measurements [16], including anterior acetabular sector angle, posterior acetabular sector angle, acetabular version angle, joint space width, lateral center-edge angle, sharp angle, alpha angle and femoral head-neck offset on sCT and CT (**instructions for measurements in Supplementary Table S1**). At the institution where the study was conducted these are standard measurements for hip morphology, used for assessment of hip dysplasia and femoroacetabular impingement. For the measurements, sCT and CT images were mixed and displayed in random order. Prior to measurements, instructions on how to measure and zoom were defined and agreed upon by the readers, in order to align their way of working (instructions provided in supplementary material). The nodes that define the endpoints of distances or angles were positioned at the outside of the cortical edge with respect to the anatomical structure. To investigate the intra-reader reliability reader 1 (L.M.) performed the measurements twice in 20 hips of 10 patients with a four-week interval to avoid recall bias. All images were evaluated using a DICOM Viewer (RadiAnt, version 4.2.1, Medixant, Poznan, Poland) and default window level.

Statistical analysis

Inter-reader, intra-reader and inter-method reliability and agreement

For each hip side, an empty linear mixed model for geometrical measurement was fitted with a random intercept for patient and a random intercept for reader (first measurement time, by method) / measurement time (second reader, by method) / method (first measurement time, by reader) to assess the inter-reader / intra-reader / inter-method reliability and agreement, respectively. The intraclass correlation coefficient (ICC) for absolute agreement, the standard error of measurement (SEM) for absolute agreement and smallest detectable change (SDC) were calculated with the estimated covariance parameters as described by de Vet et al. [17]. An interpretive scale for ICC (<0.40, poor; 0.4-0.59, fair; 0.60-0.74, good; 0.75-1.00, excellent) was also selected a priori [18]. Additionally, bias and limits of agreement were calculated with the methods of Bland and Altman.

Mean equivalence between methods

The mean geometrical angles and distances for each method (sCT versus CT) were estimated with a linear mixed model with random intercept for patient and with hip side, method, reader, and measurement time as main effects in the fixed effects part of the model. The estimated marginal means with 95% confidence interval and pairwise comparison of methods was requested. Hypothesis testing was performed at the 5% significance level. In order to prove equivalence, the two-sided 95% upper confidence limit of the mean difference between the test method, sCT, and the active control, CT, (calculated as sCT minus CT) had to be below a predefined margin [19]. This equivalency margin was defined by the lowest SDC value of both hip sides as calculated for the evaluation of the intra-reader agreement on CT. These lowest SDC values of the intra-reader agreement do not deviate from the values in the literature but are rather smaller [13, 20, 21]. All statistical analyses were performed using SPSS Statistics version 26.

**Results**

Fifty four hips from twenty seven participants (13 men, 14 women) were included for analysis. There was no reported hip pathology in the subjects.The mean age of the study participants was 40 ± 10 years (range, 20-60 years). Participant inclusion with number of measurements is summarized in **Figure 1**. Images of the hips using 3DT1MGE sequence, CT, sCT and 3D rendering of sCT are shown in **Figure 2. Figure 3** shows examples of measurements on CT and sCT. **Table 1** provides the estimated means by method. **Supplementary Table S2** displays the mean and standard deviations of sCT measurements, CT measurements and mean differences between sCT and CT per measurement, per hip side and per reader in more detail. In the Bland Altman plots in **Figure 4** (reader 1) and **supplementary Figure S1** (reader 2) the difference between the two methods are plotted against the mean score for each measurement and each reader, showing the deviations are independent of the size of the measurements.

Inter-reader reliability and agreement

The minimum ICC was excellent for all measurements except for alpha angle (fair on sCT and CT), femoral offset (fair on sCT and CT) and joint space width (fair on sCT, poor on CT). The maximum SEM value for joint space width (0.25 on sCT and 0.29 on CT) is small, indicating that the poor to fair ICC value is affected by the homogeneous sample for the joint space width [17]. The least favorable values (minimum ICC, maximum SEM and SDC) over both hips are reported in **Table 2**. All ICCs, SEMs and SDCs over both hips are reported in **Supplementary table S3**.

Intra-reader reliability and agreement

The minimum ICC was excellent for all measurements except for femoral offset (good on CT, excellent on sCT) and joint space width (excellent on CT and good on sCT). The least favorable values (minimum ICC, maximum SEM and SDC) over both hips are reported in **Table 2**. All ICCs, SEMs and SDCs over both hips are reported in **Supplementary table S3**.

Inter-method reliability and agreement

The minimum ICC was excellent for all measurements except for femoral offset (good) and joint space width (fair). The least favorable values (minimum ICC, maximum SEM and SDC) over both hips and both observers are reported in **Table 2**. All ICCs, SEMs and SDCs over both hips and observers are reported in **Supplementary table S3.**

Equivalency test

No statistically significant difference was found between sCT and CT for joint space width, femoral offset, alpha angle, acetabular version angle, anterior acetabular sector angle. For lateral center-edge angle, sharp angle, posterior acetabular sector angle some minor but statistically significant differences were found, but the mean differences were within the predefined equivalency margin (**Figure 5**).

**Discussion**

In this prospective study, we compared MRI-based synthetic CT (sCT) images and conventional CT images of the hips. The sCT images were created by a deep learning–augmented approach utilizing multiple qualitative and quantitative MRI-based tissue parameters to create quantitatively accurate synthetic CT images [8]. The equivalence statistical testing showed that all sCT measurements are equivalent to the CT measurements at the considered margins. Additionally, the observed agreement in individual morphologic hip measurements between sCT and CT, based on agreement values, also indicated a strong degree of concordance between the imaging modalities for the measurements performed. Intermethod reliability (sCT vs CT) was excellent for anterior acetabular sector angle, acetabular version angle, posterior acetabular sector angle, sharp angle, alpha angle and lateral center-edge angle. For joint space width the inter-method reliability ranged from fair to excellent and for the femoral offset from good to excellent, but the values were generally better than the inter-reader reliability values for both modalities, meaning that differences between measurements from different modalities (by a single reader) were overall better than differences between measurements performed by different readers on the same modality. This agreement suggests that sCT imaging is suitable for the measurements performed. On one hip there was an outlier between both readers for the anterior acetabular sector angle measurement due to a false tendon calcification.

 Wide variations in radiation exposure (2,75-28,04 mSv) have been reported in pelvic CT scans [22], although the amount of radiation exposure can be significantly reduced in low-dose [23] and ultra-low-dose CT [24, 25]. Recently Stern et al. [25] found that tin-filtered ultra-low-dose CT of the pelvis at a dose equivalent to standard radiographs (0,37 mSv) is adequate for assessing bone anatomy and osseous pathologies and had a markedly superior dose efficiency than standard CT. Advantages of synthetic CT over ultra-low-dose CT are the even lower (zero) dose and its ability to assess the bony and soft tissue structures of the hip in a single imaging examination. This reduces cost, time and patient discomfort when MRI is needed. Fusion of the bone and soft tissues is seamless, as the images are obtained in exactly the same scan position. Zeng et al. [26] showed another dose saving technique using deep learning for automatic segmentation of MRI-based 3D models to be as accurate as CT-based 3D-models for patients with hip diseases of childbearing age. They applied the Volumetric Interpolated Breath-hold Examination (VIBE) sequence, using one echo instead of the two echoes in the 3DT1MGE sequence of synthetic CT. This technique does not provide standard CT-like images with visualization of detailed bony structure, including trabecular lines and bone density information in HU values, as synthetic CT does. Florkow et. al. [27] recently compared synthetic CT of the hip joint with conventional CT, but was limited by the low resolution CT scans, the population of only elderly men and limited field of view not fully covering the femoral neck nor the pelvis. The measurements of joint space width and more importantly the alpha angle and femoral head-neck offset, recently highlighted as most valuable in clinical practice [16, 28], were not examined in this prior investigation. In the present study, clinically relevant measurements were analysed in a variable patient group, using thin slice CTs with similar in-plane resolution and section thickness as synthetic CT. The equivalence between CT and sCT shown in this study is very useful as quantitative measurements are of utmost importance in clinical practice, particularly for hip evaluation prior to arthroscopy. CT is currently the modality of choice for surgical planning [2, 3], but the arrival of synthetic CT derived from MR images without the need for radiation could be a game-changer in preoperative diagnosis and planning. This benefit is particularly helpful in younger patients, as they are at greater risk of developing malignancies after radiation exposure.

Our study has several limitations. Only a limited number of participants were included in this study. No patients with metal implants were included in the study, limiting the use of our technique when patients had previous operations or screw fixation. The lack of hip pathology is also a relevant drawback as patients with joint or capsular calcifications and osteoarthritis might cause problems for optimal sCT generation. The current study evaluated agreement of the entire measurement method, including differences in selection of reformat axis, image plane and selection of anatomic landmarks, all of which are sources of potential variation in the performed measurements. The original 3D T1MGE sequence was not compared with sCT in the current study because the sCT images were reconstructed from two 3D T1MGE images, which contain unique but complementary information required to generate accurate sCT images with specific bone contrast. Subsequent studies are necessary to compare sCT with conventional 3D MRI sequences for hip evaluation and preoperative planning. The MRI data were acquired with a high-performance 3-T MRI system. Future studies may be required to show that similar image quality can be achieved with MRI systems of different field strengths and different technical performance.

In conclusion, in healthy individuals we demonstrated equivalence of synthetic CT reconstructed from an axial 3DT1MGE sequence to conventional CT for the quantitative evaluation of osseous hip morphology, thus obviating the radiation exposure of a pelvic CT examination.

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**Figure 1**: Flowchart of patient inclusion.

**Figure 2**: Coronal and 3D images of the hips in a 45-year-old male (top) and a 36-year-old female (bottom). (a, b) Coronal 3 dimensional T1-weighted radio-frequency-spoiled multiple gradient echo (3DT1MGE) images. (c, d) Coronal 3DT1MGE MRI-based synthetic CT images depict the cortex better in comparison to the T1-weighted MR image. (e) Coronal CT image visualizes the cortical outline of the pelvic bone in a very comparable way. (f) 3D rendering of the MRI-based synthetic CT.

**Figure 3:** Measurements of hip morphology on CT and MRI-based synthetic CT (sCT). (a) Sharp angle (SA), (b) lateral center-edge angle (LCEA), (c) acetabular version angle (AVA), (d) anterior acetabular sector angle (AASA), (e) joint space width (JSW), (f) posterior acetabular sector angle (PASA), (g) alpha angle (AA), (h) femoral offset (FO).

**Figure 4:** In this Bland Altman plot the differences between the methods are plotted against the mean score for each measurement for reader 1. AASA= anterior acetabular sector angle, PASA= posterior acetabular sector angle, LCEA= lateral center-edge angle.

**Figure 5**: Equivalency plot depicting the outcome differences in the geometrical measurements on synthetic CT and CT. The plot indicates equivalency of sCT to CT as the entire confidence interval (red lines) is within the green equivalence band, based on the minimum smallest detectable change for the respective outcome across hips, readers and measurement times. AASA= anterior acetabular sector angle, PASA= posterior acetabular sector angle, LCEA= lateral center-edge angle.

**Figure S1:** In this Bland Altman plot the differences between the methods are plotted against the mean score for each measurement for reader 2. AASA= anterior acetabular sector angle, PASA= posterior acetabular sector angle, LCEA= lateral center-edge angle.

**Table 1: Estimated means by method on CT and synthetic CT (sCT).**

AASA= anterior acetabular sector angle, PASA= posterior acetabular sector angle

**Table 2: Inter-reader, intra-reader and inter-method reliability and agreement**

The minimum intraclass correlation coefficient (ICC), maximum standard error of measurement (SEM) and maximum smallest detectable change (SDC) over both hips and both readers is reported.

\*Poor and fair minimum ICC values. Low ICC values for joint space width correspond to small maximum SEM values, indicating the ICC value is affected by the homogenous sample for the joint space width [17]. AASA= anterior acetabular sector angle, PASA= posterior acetabular sector angle, sCT= synthetic CT

**Supplementary Supplementary table S1: Overview of methods, planes and slices for measuring.**

AASA= anterior acetabular sector angle, AVA= acetabular version angle, AA= alpha angle, FO= femoral offset, JSW= joint space width, LCEA= lateral center-edge angle, PASA= posterior acetabular sector angle, SA= sharp angle

**Supplementary table S2: Mean, SD and mean difference of synthetic CT and CT**

AASA= anterior acetabular sector angle, PASA= posterior acetabular sector angle, sCT= synthetic CT

**Supplementary Table S3: Inter-reader, intra-reader, inter-method reliability and agreement**

The intraclass correlation coefficient (ICC), standard error of measurement (SEM) and smallest detectable change (SDC) over both hips and both readers is reported.

AASA= anterior acetabular sector angle, PASA= posterior acetabular sector angle, sCT= synthetic CT