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ROLE OF DUAL ENERGY COMPUTED TOMOGRAPHY IMAGING IN GOUT

Radio-Diagnosis

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ABSTRACT

Context: Gout is a crystal induced inflammatory arthritis triggered by crystallization of uric acid in joints. The detection of urate crystals is done using polarization light microscopy after synovial fluid aspiration which is approach is invasive. Dual energy CT (DECT) is a new imaging modality that is able to identify tophi based on their chemical composition. **Aims:** To evaluate the role of Dual Energy Computed Tomography imaging in gout. **Settings And Design:** A cross sectional observational study, comprising of 30 clinically suspected patients of gout underwent DECT of all peripheral joints (including hand, wrist, elbow, ankle, foot and knee). **Methods And Material:** This study was conducted on 128 slice SIEMENS Somatom Definition Flash CT scan. A dual energy gout colour coded protocol assessed the chemical composition of the material and an automated volume assessment software, measured the monosodium urate crystal deposition volume. **Statistical Analysis Used:** Analysis was done using SPSS version 21.0. **Results:** In lower limb the MTP joint (73.33%) was commonest followed by ankle (33%) and knee (26%) with mean crystal volume of 3.51 cm3. In upper limb, MCP and PIP joints (20%) of hand are most commonly affected with mean volume of 0.24cm3. High serum uric acid (>6.4mg/dl) levels showed a positive correlation with MSU crystal deposition in all peripheral joints on DECT. **Conclusions:** DECT is useful for the diagnosis of gout in symptomatic patients. It can detect MSU crystals volume and urate burden non-invasively.

KEYWORDS

Dual energy computed tomography, Gout, ULT, MSU crystals.

INTRODUCTION

Gout is a crystal induced inflammatory arthritis and results from deposition of Monosodium Urate (MSU) crystals within joints and soft tissues when urate concentration increases above physiological saturation limit (6.4mg/dl).[1] Inspite of its high prevalence in the world, there is still a significant diagnostic delay resulting in increased morbidity as early diagnosis and treatment is essential to prevent complications and to reduce long term disability.

The gold standard for detection of urate crystals is polarization light microscopy after synovial fluid aspiration however this approach is invasive.[2,3] It has complications like bleeding, infection, damage to adjacent structures and inadequate specimen from small joints or periarticular structures , and hence this procedure is reserved for diagnostic dilemmas.[4] It is not preferred as small joints are inaccessible for aspiration and polarization microscopy has limited sensitivity of 70%.

Imaging techniques are useful for detection of urate crystals deposition in early disease process even before first clinical symptoms. Plain radiographs can be normal at first presentation and sensitivity for detection of gout is only around 30%.[5]

Sonography can detect joint effusion in early phase with echogenic mobile urate crystals producing a “starry sky” appearance with characteristic “Double contour” sign. USG is an inexpensive diagnostic tool but there is no standardized scanning technique and sometimes extensive scanning is required so it cannot be used accurately on large scale.

MRI is an important imaging investigation due to its high soft tissue resolution and lack of ionising radiation however it is very expensive and not available on large scale.

Dual energy CT (DECT) is relatively new imaging modality that is able to identify tophi based on their chemical composition and shows great potential in the diagnosis of gout and quantification of tophi burden. It helps avoid an invasive procedure and prevent complications. It can also help in monitoring disease progression and response to therapy thus easily conveying urate burden to non radiologists also.

MATERIAL AND METHODS

A cross sectional observational study was conducted in the Department of Radiodiagnosis at ABVIMS & Dr. Ram Manohar Lohia Hospital, Delhi from 1 November 2018 to 31 March 2020 . 30 clinically suspected patients of gout based on American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) 2015 Criteria attending Rheumatology clinic were enrolled in the study.

Inclusion Criteria:

Clinically diagnosed patients of gout.

Exclusion Criteria:

Pregnant patients.

CT Evaluation

DECT scan was performed on 128 slice SIEMENS Somatom Definition Flash CT scan. Non contrast scan was done. Using a dual energy gout colour coded protocol that specifically assess the chemical composition of the material, scan of all peripheral joints was done (including hand, wrist, elbow, ankle, foot and knee). Post-processing was done using a commercial software programme ('Gout', Syngo CT Workplace, Siemens Medical Systems) to form selective images, MSU crystals were coded as green. The appearance of green-coloured voxels in articular or periarticular locations was diagnosed as positive for the presence of MSU crystals. Using an automated volume assessment software the monosodium urate (MSU) crystal deposition volume was measured.

Statistical Analysis

The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0. Inter-rater kappa agreement was used to find out the strength of agreement between clinical findings, serum uric acid levels and urate crystal deposition on DECT.

RESULTS:

Among the 30 patients the maximum number of patients belonged to the 40-60 year old age group (70%) and most of them were males (76.67%).28 patients (93.33%) presented with clinical symptoms and out of which pain (93.33%) in joints being the most common followed by erythema and tenderness. Most of the patients (76.67%) presented after 6 weeks with recurrent disease in comparison to 7 patients (23.33%) who presented before 6 weeks. The most common joint involved in our study population in lower limb was MTP joint (66.67%) followed by ankle (56.67%) and knee (43%). In upper limb,

MCP and PIP joints of hand are most commonly affected followed by wrist and elbow joint. 53.33% patients were positive for CRP and 43.33% patients were positive for ESR. 24 out 30 (80%) patients were negative for RA factor. 16 out of 30 (553.33%) patients showed punched out erosions and tophi deposition in joints.

The most common joint involved in our study population in lower limb was MTP/foot joint (73.33%) followed by ankle (33%) and knee (26%). (Figure 1) Among 22 positive patients for crystals, the mean value being 3.51 cm^3 ranging from 0 to 29.97cm^3 in lower limb. In upper limb, MCP and PIP joints (20%) of hand are most commonly affected with mean value of 0.24 cm^3 and ranging from 0 to 4.23 cm^3.(Figure 2)

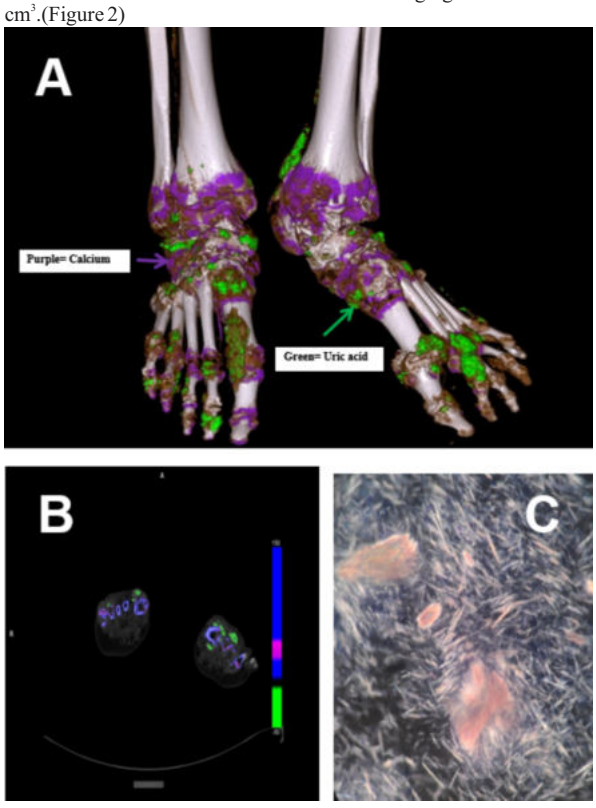

Figure1 A 3D and axial colour coded post processed images demonstrate scattered MSU deposits in intra-articular and periarticular region within tendons in bilateral feet in green colour. Purple represents calcium.
B DECT reveals a large tophi in bilateral 1st and left 2nd MTP joints with underlying bony erosions.
C Polarizing microscopy demonstrates needle shaped birefringent urate crystals in these deposits.

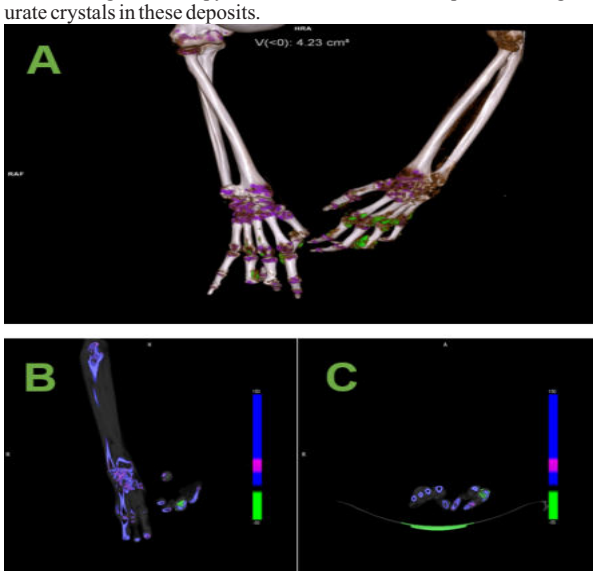

Figure 2 A 3D volume rendered images depicting tophi in left MCPs and 4th PIP joint. Scattered MSU crystals are also seen in bilateral hand and right wrist joint (Volume 4.23cm3).
B and C Coronal and axial DECT with colour mapping images show uric acid crystals in green, consistent with gouty arthritis.

High serum uric acid (>6.4mg/dl) levels shows a positive correlation with MSU crystal deposition in all peripheral joints on DECT , p value being 0.019 and kappa being 0.392 showing a fair interob server kappa agreement. The clinical findings did not show any significant correlation with MSU crystals on DECT.

DISCUSSION

DECT is a non invasive tool that can confirm the diagnosis of gout and also help in monitoring of appropriate treatment response by quantifying crystal deposition. The colour display and 3D volume rendered imaging allows information to be clearly communicated to clinicians and patients. The objective of this study was to assess the role of DECT in diagnosing gout and to provide quantification of urate burden**.** This study also describes correlation between serum uric acid levels and MSU crystal deposition on DECT.

Demographic Profile

The maximum number of patients (70%) belonged to 40-60 year age group. There was a male predominance seen in all age groups. Gout is uncommon in young premenopausal women due to uricosuric effect of oestrogen[6]however incidence of gout increases after menopause.

Distribution Of Disease Duration

76.67% patients presented with chronic (>6 weeks) recurrent disease and 23.33% were acute cases. Among acute cases, only 28.4% (2 out of 7) patients showed urate deposition on DECT. Among patients with chronic course of disease, 86.9% (20 out of 23) patients showed urate crystals on DECT. Thus DECT has limited role in acute cases of gout.

Clinical Parameters

92% (28 out of 30) of the patients presented with clinical symptoms with pain being the most common followed by erythema and tenderness. The most common presenting joint was MTP joint (66.67%) followed by ankle (56.67%) , knee(43.33%), MCP/ PIP/Hand (36.67%), wrist (20%) and elbow joint (13.33%). As compared to upper limb, lower limb is more commonly involved and first MTP joint is most commonly involved among overall joints.(figure 3)

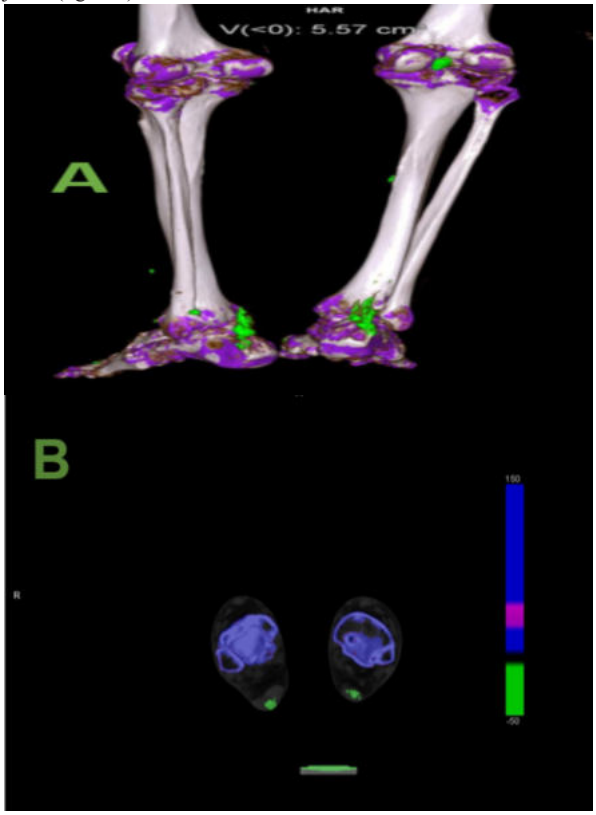

Figure3 Dual energy CT (DECT) images of patient with suspected

gout

A 3D DECT reconstruction and B. 2D axial images , uric acid deposition seen in bilateral achilles tendon depicted in green. Smaller tophaceous deposits are also distributed throughout the lower limb joints bilaterally.

The clinical findings in our study did not show any significant correlation with MSU crystals on DECT. In those patients of clinically diagnosed gout with negative DECT findings, clinicians were suggested to modify the ULT (Urate lowering therapy) regime. Thus DECT increases the confidence of clinicians to initiate or discontinue ULT regime.

Imaging Features On CT: Punched Out Erosions And Tophi Distribution

In our study, 53.33% (16 out of 30) patients had typical extramarginal or articular punched out erosions with overhanging sclerotic margins with relatively preserved joint space. All the patients in our study with punched out erosions have associated tophi deposition.(Figure 4) Thus a positive correlation has been found between MSU crystal deposition and formation of bony erosions.

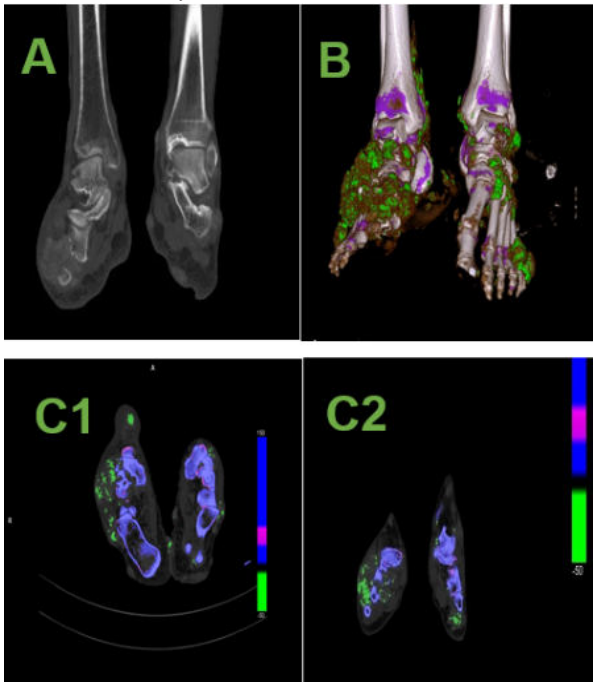

Figure 4 37 year old man with bilateral feet and ankle pain
A Coronal 2D CT image of bilateral ankle and feet shows high attenuation tophi with typical punched out bony erosions in left distal tibia , bilateral talus , navicular , intermediate cuneiform and right 4th MTP joint .
B 3D DECT reconstruction shows uric acid deposits (green) in periarticular and articular tissues of bilateral ankle and feet.
C1,C2 2D coronal and axial images with colour mapping shows uric acid deposition in green.

Distribution Of MSU Crystals Deposition

Amongst all the joints evaluated seperately for urate crystal deposition on DECT, MTP/foot joints (73.34%) were most commonly involved followed by ankle (33.33%) and knee joints (26.66%). MCP/PIP/hand (20%) and wrist joints (10%) were less commonly affected with no involvement of elbow joint in any patient .The mean urate crystal volume in lower limb peripheral joints was 3.51 cm^3 ranging from 0.01 to 29.97 cm^3 and in upper limb peripheral joints was 0.24 cm^3 ranging from 0.01 to 4.23 cm^3

For detection of MSU crystal deposition, DECT needs atleast 12.5% concentration of urate crystals. The minimum value of at least 15% to 20% MSU by volume and size of at least 2 mm is required for identification of tophus.[7]

Subclinical Urate Burden

DECT is helpful in diagnosing urate crystals in locations and joints other than the symptomatic joint which has subclinical urate deposition.

Follow Up DECT After Urate Lowering Therapy

In our study the mean urate crystal volume in lower limb peripheral joints was 3.51 cm^3 ranging from 0.01 to 29.97 cm^3 and in upper limb peripheral joints was 0.24 cm^3 ranging from 0.01 to 4.23 cm^3. Follow up scan was done in 5 patients on ULT after a period of 3-9 months and all of them showed reduction in urate volume on serial DECT scan .The mean volume of reduction was 3.5 cm^3.(Figure 5)

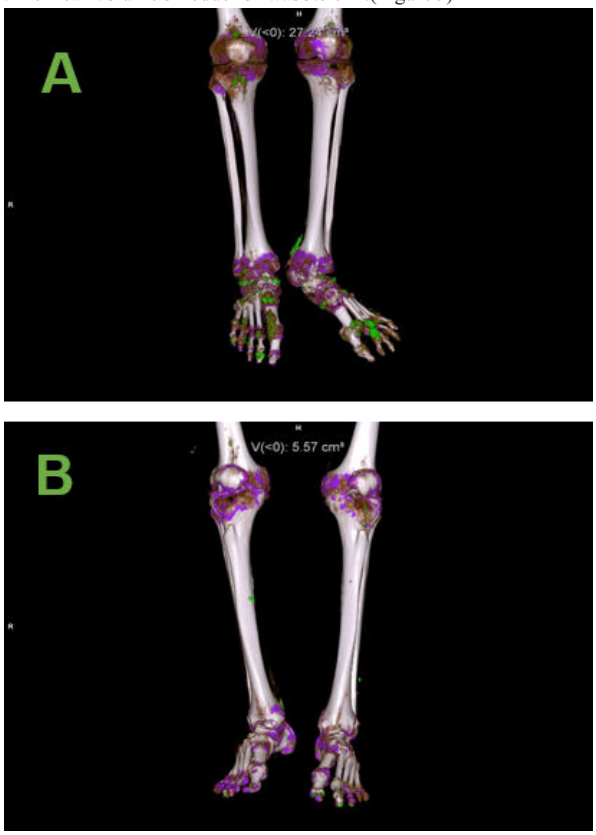

Figure 5 A Initial DECT revealed multiple tophi in both feet, ankle and knee joints (Volume 27.24 cm3).
B Follow-up 3D DECT at 9 months after treatment showed significant improvement and resolution of urate crystals, suggestive of response to treatment (Volume 5.57cm3).

MSU Crystal Deposition In Extra-Articular Tissues

Extra-articular sites were involved in 26.66% (8 out of 30) patients. Out of which, 4 patients had urate deposition in achilles tendon, 2 patients around peroneal tendons and 2 patients had in the region of popliteal tendon in knee. Entheses are a frequent location for urate deposition in patients with a negative synovial aspirate.

False Positives And False Negatives In DECT

DECT should be interpreted carefully by an expert who is well trained to identify artifacts. Most common locations for artifacts are skin, calluses, nail bed and around arthroplasties and implants but most of the time they are easy to identify based on location .False positive results are also seen in patients with high grade osteoarthritis.[8] (Figure 6) DECT can have false-negatives also in cases of acute gout when size of tophi is too small to be detected .

Correlation Between MSU Crystals And Serum Uric Acid Levels

In our study, 60% (18 out of 30) patients were on antihyperuricemic drugs. There is a significant positive correlation between urate crystal deposition and high serum uric acid levels (>6.4mg/dl) with p value of 0.019 and kappa of 0.392 showing fair inter observer kappa agreement. In 2 patients, urate crystals were noted on DECT even in the absence of hyperuricemia. DECT can also detect urate crystals in normouricaemic patients without any evidence of tophi.[9]

DECT Vs Other Imaging Modalities For Diagnosing Gout

Deposition of MSU crystals, presence of tophi, soft tissue swelling

accompanied by typical punched out bony erosions with overhanging margins and preservation of joint space are classical findings of gout. Plain radiographs[10] have been used as the initial investigation in patients of suspected gout. They are usually normal at the time of initial presentation and the sensitivity for the detection is only 30%.[11]

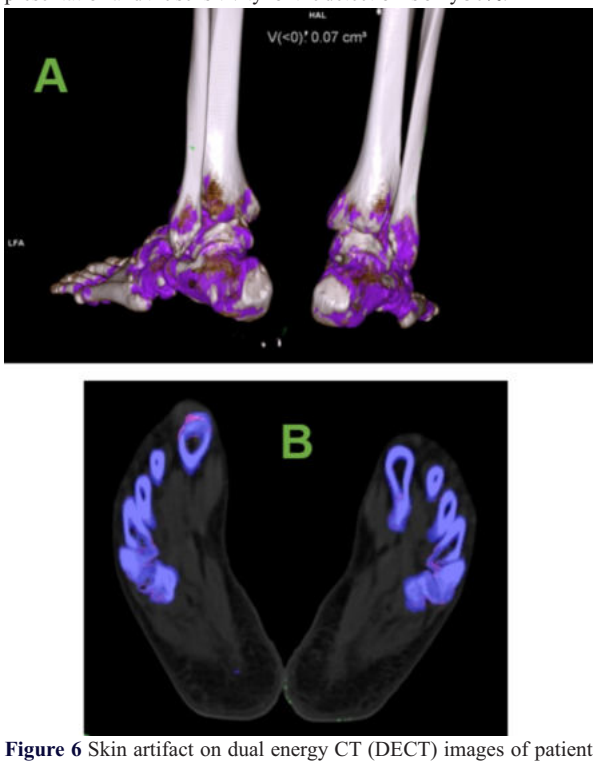

Figure 6 Skin artifact on dual energy CT (DECT) images of patient with suspected gout.
A Skin artifact (arrow) is seen in skin over calcaneal region on 3D DECT reconstruction.
B Skin artifact (arrow) is seen in calcaneal region on axial DECT image of the same patient.

The **'double contour'** sign on ultrasound is an early sign with sensitivity ranging from 25-95% and is seen in patients with asymptomatic hyperuricemia. It definitely has a role in early diagnosis of gout but intraosseous deposits are difficult to diagnose on USG and it also underestimates the number and extent of erosions as compared to CT.[11] (Figure7)

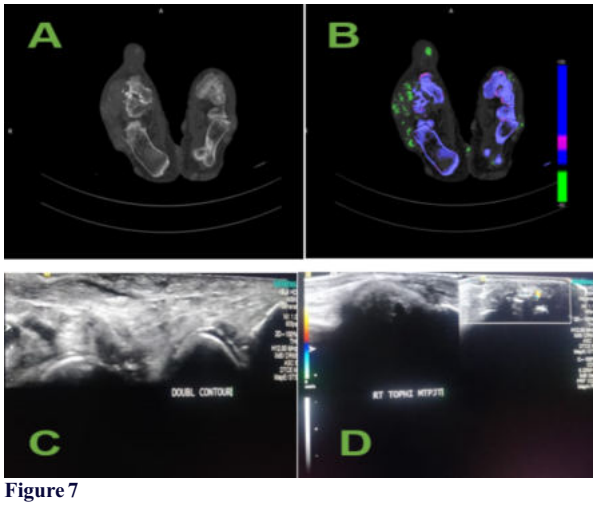

Figure 7
A. 2D axial CT image shows high density material in soft tissue within and in surrounding joints , consistent with tophaceous deposits with underlying punched out lytic bony erosions B. 2D axial DECT green coloured urate deposits in and around the erosions.
C.Utrasound image showing two parallel hyperechoic contours (bone and uric acid deposition) on either side of hypoechoic hyaline cartilage – Double contour sign.
D. Tophus is demonstrated in ultrasound image of right 1st MTP joint.

MRI is usually not preferred in the evaluation of crystal arthropathies because it is less sensitive for detection of crystals. Another drawback is limited MRI availability and comparatively high cost, its use is limited to specific joint evaluation thus subclinical gout in other joints can be missed.[12]

DECT is very sensitive and accurate in diagnosing urate crystal deposition, bony erosions and tophi burden. It can detect urate deposition in cases of subclinical gout as well. (Figure 8) DECT is considered better than MRI as the slice thickness (as low as 0.5 mm) is considerably thinner than that of MRI (commonly 2.5 to 4 mm) and there is no gap between the slices as they can be reconstructed in overlapping manner for 3D reformatting purposes. CT scan has another major advantage over MRI as larger regions can be scanned and the pattern of joint involvement can be easily evaluated.[10]

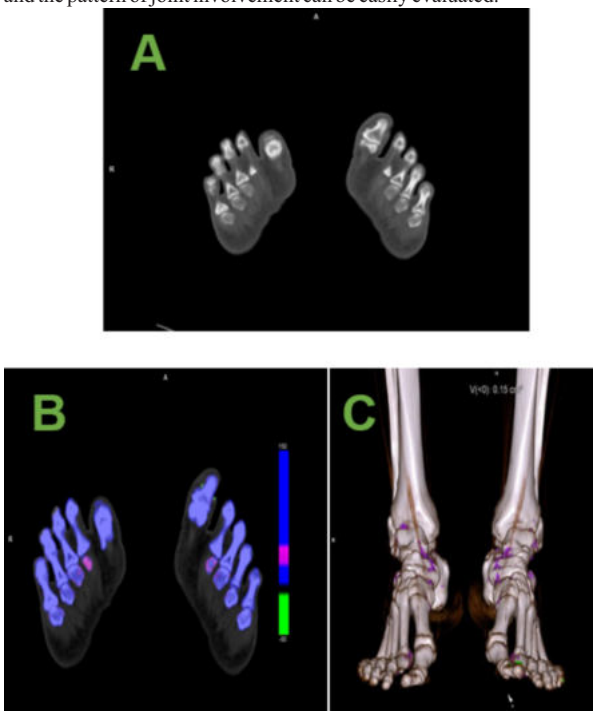

Figure 8 AA negative axial CT with no findings of gout.
B Subtle uric acid deposition seen on 2D axial DECT image in a patient with mild symptoms.
C 3D volume rendering DECT image of the same patient shows volume of urate crystals (Volume 0.15cm3) .

DECT vs Other Imaging Modalities For Monitoring Response To Treatment

Direct quantitative volume measurement of MSU crystals can be made on DECT, so even asymptomatic patients and patients showing mild changes in tophus load can be recorded with excellent reproducibility on sequential DECT scans.[11] US can only detect subcutaneous and periarticular tophi and it is operator-dependant so tophi burden cannot be assessed completely in all the joints including joints with subclinical urate crystals. Due to better imaging and soft tissue resolution, MRI and CT diameters are usually larger than that of US. Thus CT and MR imaging have better sensitivity and specificity for diagnosis and measurement of tophi burden.

Drawbacks Of DECT

DECT has few drawbacks as it is costly and exposes the patient to radiation. However the amount of radiation ranges from 2 to 3 mSv which is comparable to standard CT scan. Both false-positive and false-negative results can occur because of artifacts and it has limited role in advanced osteoarthritis.[13]

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