Digital tomosynthesis for bone erosion scoring in gout: comparison with plain radiography and computed tomography

Sir, CT is the current gold standard for the assessment of bone erosion in inflammatory arthritis [1]. However, CT is costly and requires large radiation doses. Digital tomosynthesis is a recently developed imaging method in which multiple projected images obtained at different angles are collected with a digital detector [2, 3]. These cross-sectional images are used to reconstruct three-dimensional images of the scanned object. Several recent studies have reported that tomosynthesis allows low-cost, low-radiation detection of bone erosion in RA [4, 5].

Bone erosion is a frequent complication of tophaceous gout. The radiographic appearance of gouty erosions differs from that of RA, with sclerotic edges, overhanging margins and preserved periarticular bone [6]. The aim of this study was to determine the sensitivity and reproducibility of digital tomosynthesis compared with plain radiography (XR) and CT for the scoring of bone erosion in gout.

Thirty-six people with gout were prospectively recruited from rheumatology outpatient clinics in Auckland, New Zealand (97% male, mean disease duration 18 years, 78% with s.c. tophi). All participants had gout according to the 1977 ARA classification criteria. XR and CT scans of the dominant wrist were obtained as previously reported [7]. Tomosynthesis was performed on the same day using a commercially available tomosynthesis unit (Volume RAD, GE Medical Systems, Pewaukee, WI, USA) (Fig. 1). A coronal projection was acquired, with the X-ray tube moving in an arc of 40° relative to a fixed solid-state detector. Focal spot size was 0.6 mm. The exposure factors were a tube voltage of 50 kV and current of 100 mA with a total exposure time of 6.3 s. The tomographic layer height was 35 mm, yielding 30 partitions of 1-mm nominal thickness. This study was approved by the New Zealand Ministry of Health Ethics Committee. All patients provided written informed consent according to the Declaration of Helsinki.

Each image was scored separately by at least two readers for bone erosion using semi-quantitative volume assessment using sites and scoring as for the RA MRI score erosion method for the wrist [8]. XR scores were scored by a musculoskeletal radiologist [A.G. (reader 1)] and a rheumatologist with experience in scoring XRs [N.D. (reader 2)]. The tomosynthesis images were scored by three musculoskeletal radiologists [reader 1, M.R. (reader 3) and A.D. (reader 4)] and the CT images were scored by two musculoskeletal radiologists (readers 1 and 3). All images were scored separately without reference to the other scans and each reader was blinded to all other readers’ scores.

Data were analysed using SPSS version 21 (SPSS, Chicago, IL, USA) and GraphPad Prism version 5 (GraphPad Software, La Jolla, CA, USA). Interobserver reproducibility was assessed by intraclass correlation coefficient (ICC). Differences between XR, tomosynthesis and CT scores were analysed using repeated measures one-way analysis of variance (ANOVA) with Bonferroni post hoc tests. Pearson’s correlations were used to examine the relationship between scores using different imaging methods.

The two-reader ICC for the erosion score was 0.86 (95% CI 0.74, 0.93) for XR (readers 1 and 2) and 0.81 (95% CI 0.65, 0.90) for CT (readers 1 and 3). The three-reader ICC for tomosynthesis was 0.67 (95% CI 0.50, 0.80). For tomosynthesis, the two-reader ICC for readers 1 and 3 was 0.62 (95% CI 0.37, 0.78), for readers 1 and 4 was 0.90 (95% CI 0.80, 0.95) and for readers 3 and 4 was 0.64 (95% CI 0.40, 0.80).

The mean erosion scores were 6.9 (s.d. 8.8) for XR and 13.6 (s.d. 15.3) for CT. For tomosynthesis, the three-reader mean erosion score was 9.1 (s.d. 11.7). Erosion scores were significantly different between the three readers [mean scores: for reader 1, 5.1 (s.d. 7.9); for reader 3, 16.3 (s.d. 19.5); for reader 4, 5.8 (s.d. 9.2); ANOVA P < 0.0001, Bonferroni P < 0.0001 for reader 3 compared with both readers 1 and 4].

For the reader who scored all images (reader 1), the mean XR score was 6.4 (s.d. 9.1), tomosynthesis score was 5.1 (s.d. 7.9) and CT score was 12.2 (s.d. 13.3). CT scores were significantly higher than both XR and tomosynthesis, with no difference between XR and tomosynthesis scores (ANOVA, P < 0.0001; Bonferroni XR vs CT, P < 0.0001; tomosynthesis vs CT, P < 0.0001; XR vs tomosynthesis, P > 0.05). For reader 1 there was a high correlation between XR, tomosynthesis and CT scores (XR and tomosynthesis r = 0.94, tomosynthesis and CT r = 0.88, 9.8, and CT and XR r = 0.93, P < 0.0001 for all).

This study has shown that tomosynthesis has variable reproducibility and does not confer advantage over XR for the measurement of erosion burden in gout. Our findings differ from RA studies, which have shown excellent reproducibility and increased detection of erosion burden compared with XR [4, 5]. It is possible that the different physical characteristics of the erosions in RA and gout explain this variation. It is also possible that tophus deposited within the gouty erosion may obscure the edges of the erosion [7], leading to lower reproducibility and detection of erosion. Analysis of tomosynthesis in other forms of erosive arthritis will be of interest. Our data do not support the usefulness of digital tomosynthesis in the quantification of bone erosion in gout.
Digital tomosynthesis has variable reproducibility without advantage over plain radiography for the measurement of gouty erosions.

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**References**


**Multiple upper gastrointestinal perforations in a 15-year-old patient treated with tocilizumab**

**Sir,** Tocilizumab, an IL-6 receptor antagonist, has been approved for treatment of RA and systemic and polyarticular JIA [1–3]. Tocilizumab appears to have an acceptable safety profile [4], however, gastrointestinal perforation was reported as a rare but severe complication in tocilizumab therapy [5]. This severe side effect seems to be associated specifically with tocilizumab treatment and has not been reported for other biologics [6]. Gastrointestinal perforations have so far only been reported in adults, while older age and pre-existing diverticulitis were found to be the strongest risk factors associated with perforation [7]. We recently managed an adolescent patient who experienced multiple perforations in the terminal ileum after receiving tocilizumab therapy for systemic JIA (sJIA).

A 15-year-old boy developed oligoarthritis of the knees and ankles in June 2011. At first presentation he had markedly elevated inflammation parameters (ESR 52 mm/h, CRP 13.3 mg/dl), ANA and RF were negative and HLA-B27 was positive. Hence our patient fulfilled the criteria for enthesitis-associated JIA. During the following months, treatment with steroids, NSAIDs and MTX did not result in lasting remission and any attempt to reduce the prednisone dose to <0.5 mg/kg body weight resulted in prompt clinical deterioration. Gastroscopy and colonoscopy, which were conducted in September 2011 due to the persistence of intense inflammation signs, showed no pathological findings.

During subsequent months the patient developed intermittent fever episodes and progressing arthritis. This made us suspect systemic rather than enthesitis-associated arthritis, and we finally initiated tocilizumab therapy in May 2012. Two days later the patient reported gastrointestinal pain and diarrhoea. Gastroscopy and colonoscopy were repeated. Only minor inflammation was seen in the distal ileum and histology revealed a non-specific inflammation in the terminal ileum and distal colon.