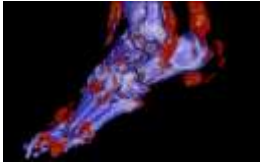


Assessment of Tophus Size: a Comparison Between Physical Measurement Methods and Dual Energy Computed Tomography Scanning

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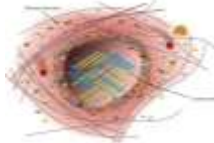
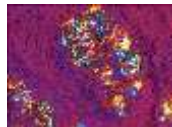


Disclosures

- This work was funded by the Health Research Council of New Zealand
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- I have no other relevant financial disclosures.

Background

- The tophus is a pathognomonic feature of gout
- Foreign body granulomatous response to monosodium urate (MSU) crystals
 - Innate and adaptive immune activation



Dalbeth *Arthritis Rheum* 2010

Background

- Impact of tophi
 - Disfiguring
 - Discharge with secondary infection
 - Obstruct joint movement
 - Disability
 - Joint damage
- Tophus regression has been endorsed by OMERACT as a core domain for clinical trials of chronic gout



Schumacher *J Rheumatol* 2009

Background

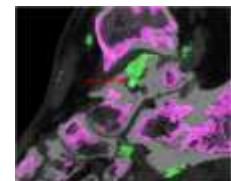
- Many methods of tophus measurement described:
 - Vernier calipers (longest index tophus diameter)*
 - Tape measurement (index tophus area)
 - Counting of all visible tophi
 - Digital photography
 - Ultrasonography
 - Magnetic resonance imaging
 - Conventional computed tomography (CT)

*OMERACT endorsed

Dalbeth *ARD* 2011

Background

- Dual energy CT (DECT) is a sensitive and specific method to detect urate deposits in patients with gout
- DECT uses a specific display algorithm that assigns different colours to materials of different chemical composition (such as urate and hydroxyapatite)
- The reliability of DECT for tophus measurement has not been reported to date



Choi *ARD* 2009
Glazebrook *Radiology* 2011

Aim

- To compare the reliability and validity of various physical methods with DECT assessment of tophus size

Methods: physical measurement

- Each tophus was assessed by two independent observers
 - Vernier calipers (longest diameter)
 - Tape measure (area)
- Tophus location was recorded in detail using a diagram and written description
- The total number of subcutaneous tophi was also counted
- Five patients returned within one week for repeat physical assessments

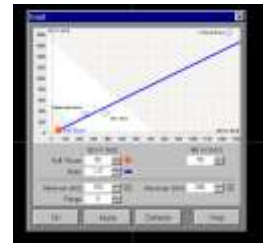


Methods: patients and tophus selection

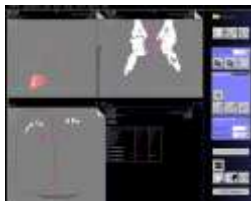
- Twenty-five patients with
 - a history of acute gout according to ACR classification criteria, and
 - at least one subcutaneous tophus
- For each patient, up to three index tophi were selected for analysis (n=64 tophi, 55 in the feet)
 - sites in the feet were preferentially selected
 - if >3 tophi present in the feet, the largest tophi were selected
 - discharging, acutely inflamed or bursal tophi were not selected

Methods: DECT

- All patients proceeded to DECT scanning of both feet (Somatom Definition Flash, Siemens Medical)
- Index tophus DECT volume was assessed by two independent observers using automated volume assessment software
- DECT scans from the returning patients were scored twice by both observers



Methods



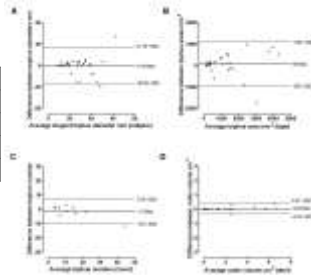
- Each observer was blinded to the scores of the other observers and previous measures
- Intra- and inter-observer reproducibility was assessed by intraclass correlation coefficient (ICC) and limits of agreement analysis (Bland and Altman).
- For the purposes of these analyses the unit of investigation was assumed to be the tophus

Results: patient characteristics

Variable	All patients (n=25)	Patients returning for second visit (n=5)
Age, years, median (range)	64 (40-85)	64 (44-74)
Male gender, n (%)	23 (92%)	5 (100%)
Ethnicity, n (%)		
Pacific	10 (40%)	2 (40%)
New Zealand Maori	1 (4%)	0 (0%)
New Zealand European/Other	14 (56%)	3 (60%)
Aspirate proven gout	11 (44%)	2 (40%)
Gout disease duration, years, median (range)	24 (3-50)	45 (21-49)
Serum urate, mmol/L, median (range)	0.39 (0.18-0.71)	0.37 (0.35-0.49)
On allopurinol, n (%)	18 (72%)	4 (80%)
Total DECT urate volume (both feet), cm ³ , median (range)	1.65 (0.07-28.88)	8.02 (0.13-28.88)

Results: Intraobserver reproducibility (Assessment 1 vs. Assessment 2)

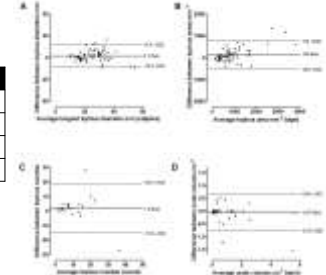
	ICC, mean (95% CI)
A Vernier calipers	0.75 (0.54-0.87)
B Tape measure	0.91 (0.82-0.96)
C Tophus count	0.94 (0.77-0.98)
D DECT volume	1.00 (0.99-1.00)



To allow comparison between measures, the y axis value approximates twice the mean score.

Results: Interobserver reproducibility (Observer 1 vs. Observer2)

	ICC, mean (95% CI)
A Vernier calipers	0.78 (0.66-0.86)
B Tape measure	0.88 (0.82-0.93)
C Tophus count	0.58 (0.25-0.79)
D DECT volume	0.95 (0.92-0.97)



To allow comparison between measures, the y axis value approximates twice the mean score.

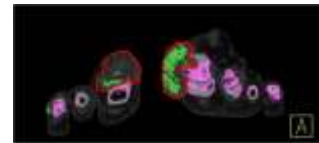
Results: Comparison of values between different methods (feet, n=55)

	Calipers	Tape
Calipers	-	$r_s=0.94$ $p<0.0001$
Tape	$r_s=0.94$ $p<0.0001$	-
DECT	$r_s=0.46$ $p=0.004$	$r_s=0.46$ $p=0.004$

- In 20% of tophi recorded on physical assessment, no urate deposits were observed in the tophus by DECT
- Those tophi without urate deposits on DECT had smaller caliper diameter ($p=0.02$) and tape area ($p=0.01$)

Results: distribution of urate in tophi

- Large variation was observed in the amount of urate deposits documented by DECT in tophi of similar physical size
- Discrete urate collections were frequently scattered throughout the tophus, typically surrounded by soft tissue



Example of two similar sized tophi from a single patient showing large variation in urate volume. The borders of the tophi (determined from CT images) are outlined.

Summary

- DECT reveals the composition of tophi which contain variable urate deposits embedded within soft tissue
- DECT scanning is a highly reproducible method of assessing urate load within tophi
 - Overall higher reproducibility than physical tophus measurement methods
 - Relatively modest relationship between physical tophus size and DECT urate volume, reflecting the composition of the tophus

Further questions/issues

- Is DECT sensitive to change?
- Is DECT feasible for use in clinical trials?
 - Cost
 - Availability
 - Radiation
- What is the relative importance of urate load compared with total tophus size on clinically relevant outcomes?