# Quantifying Erosions in Rheumatoid Arthritis Patients Using The EERA Software

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## ABSTRACT

***Background.*** That magnetic resonance imaging (MRI) captures bone erosion at an earlier stage of rheumatoid arthritis (RA) than conventional imaging modalities has been known since the field work of Gilkeson et al. in 1988. Instruments designed to capture the clinical relevance of such findings, as is the case with the Outcome Measures in Rheumatology Committee RA MRI scoring system, have been set-back by inconsistency in both intra and inter-rater reliability. Semi-automating erosion quantification poses one approach to increase reliability across readers. The developed *Early Erosions in Rheumatoid Arthritis* (EERA) software is a semi-automated approach which seeks to quantify RA patient erosions using an amalgamation of conventional Region Growing and Level-Set Segmentation algorithms. The principle aim of this study was to determine intra and inter-rater reliability when applying EERA software to the quantification of erosions in the metacarpal phalanges (MCPs) of RA patients.

***Methods.*** Two readers, R1 and R2, trained in the use of EERA software but otherwise inexperienced with conventional quantification techniques evaluated erosions captured by MRI in the second through fifth MCPs of 50 patients diagnosed with RA under the American College of Rheumatology 1987 revised definition. A 1T magnet, 100mm diameter cylindrical transmit and receive coil, and a 3D spoiled gradient echo sequence were used in acquiring the images. Images were evaluated by each reader twice with a 72 hour wait period between runs. Intra and inter-rater reliabilities for the total volume measures between the two readers and between two runs were assessed via intra-class correlations, ICC(2,1), with 95% confidence intervals. For runs one and two, volume measures from each reader were graphed against each other in Bland-Altman difference plots so as to visually capture the degree to which scores varied.

***Results.*** Of the 50 participants recruited for the study, 16 were males and 34 were females. Study subjects had a mean age of 57 (SD=11.5), a mean weight of 78 kg (SD=15.6), and a mean height of 169 cm (SD=13.9). Readers identified 64 ± 1 erosions in the patients: 15 of these occurred in second MCP, 33 ± 1 occurred on the third MCP, 12 ± 1 occurred in the fourth MCP, and 4 occurred in the fifth MCP. The mean erosion size as determined by R1 during the first and second run were 87.9mm$^3$ (SD=118.9) and 88.1mm$^3$ (SD=121.2) respectively. R2's measures had a mean erosion volume of 90.7mm$^3$ (SD=130.1) for the first run and 103.2mm$^3$ (SD=151.0) for the second run. For both runs, agreement between readers was better for smaller sized erosions decreasing appreciably beyond 100mm$^3$ (See Figure 1. Run 2 results not shown but are available upon request). The intra-rater reliability had an ICC value of 0.956 with a 95% confidence intervals ranging from 0.935 to 0.970. Between R1 and R2, the inter-rater reliability had an ICC value of 0.921 with a 95% confidence interval from 0.886 to 0.946.

***Conclusion.*** Results obtained suggest that EERA software can be applied to acquire MCP erosion volume measures in a reliable manner.

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## INTRODUCTION

The presence of erosions on radiographic data has long been used as an indicator of disease extent and progression in rheumatoid arthritis (RA) (1). That magnetic resonance imaging (MRI) captures bone erosion at an earlier stage of rheumatoid arthritis (RA) than conventional imaging modalities has been known since the field work of Gilkeson et al. in 1988. Instruments designed to capture the clinical relevance of such findings, as is the case with the Outcome Measures in Rheumatology Committee RA MRI scoring system, have been set-back by inconsistency in both intra and inter-rater reliability. Semi-automating erosion quantification poses one approach to increase reliability across readers.

The recent work by Emond et al. provides a novel approach for semi-automating the measure of bone erosions (2). The developed *Early Erosions in Rheumatoid Arthritis* (EERA) software is an amalgamation of conventional Region Growing and Level-Set Segmentation algorithms using mathematical logic operators (2). In hybridizing these two algorithmic techniques, weaknesses associated with each, including the inability to capture erosion of small radiant intensities or poor delineation, are offset by the respective counterpart component. Herein, we seek to determine the feasibility of applying EERA software in a reliable manner to capture erosions in the metacarpal phalanges (MCPs) of RA patients.

## METHODS AND MATERIALS

### *Patient Recruitment & Selection Criteria*

A 2009-2010 database containing MR MCP images from patients diagnosed with RA under the American College of Rheumatology 1987 (3) revised definition was accessed (See Table 3. and Table 4. Patient Demographics). All images were acquired at the Centre for Appendicular MRI Studies (CAMRIS) in Hamilton, Ontario with patients being recruited from the surrounding area. Scans collected at the CAMRIS are part of an ongoing study which seeks to monitor progression of RA as measured by MRI and standard radiographic techniques.

### *Segmentation*

Two readers, R1 and R2, trained to use EERA software but otherwise inexperienced with conventional quantification techniques evaluated erosions captured by MRI in the second through fifth MCPs of 50 patients diagnosed with RA under the American College of Rheumatology 1987 revised definition (See Figure 3.). A 1T magnet, 100mm diameter cylindrical transmit and receive coil, and a 3D spoiled gradient echo sequence were used in acquiring the images (See Table 1. MR Imaging Parameters). Images were evaluated by each reader twice with a 72 hour wait period between runs. Intra and inter-rater reliabilities for the total volume measures between the two readers and two runs were assessed via intra-class correlations, ICC (2,1), with 95% confidence intervals. Statistical analysis was performed using MedCalc software (Version 12, Belgium). For runs one and two, volume measures from each reader were graphed against each other in Bland-Altman difference plots so as to visually capture the degree to which scores varied.

## MR IMAGING PARAMETERS

| | |
|---|---|
| Repetition Time | 60.0ms |
| Echo Time | 7.6ms (minimum) |
| Slice Thickness | 1.0mm |
| Average Number of Slices | 32.5 Slices |
| Minimum Number of Slices | 24 |
| Maximum Number of Slices | 44 Slices |
| Imaging Matrix | 256x512 Re-sampled to 512x512 |
| Field of View | 140x140mm |
| Voxel Dimensions | 0.273x0.273x1.0mm |
| Number of Averages | 1 |
| Imaging Coil | 100 mm cylindrical |
| Flip Angle | 60.0° |
| Bandwidth | 50kHz |

**Table 1.** MR Imaging Parameters

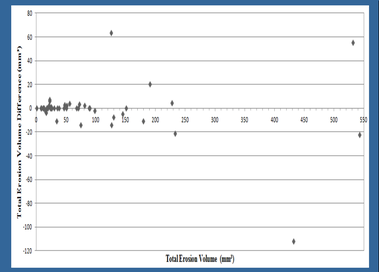


**Figure 1.** Run 1 Reader Measured Total Erosion Volume Differences Plotted Against Increasing Volume Size.

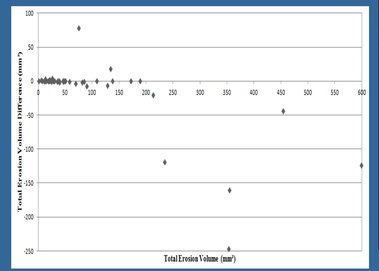


**Figure 2.** Run 2 Reader Measured Total Erosion Volume Differences Plotted Against Increasing Volume Size.

## PATIENT DEMOGRAPHICS

| Variable | N | Mean | SD | Minimum | Maximum |
|---|---|---|---|---|---|
| Age (yr) | 50 | 57.6 | 11.5 | 32 | 86 |
| Weight (kg) | 43 | 77.7 | 15.6 | 50 | 118 |
| Height (cm) | 42 | 169.2 | 13.9 | 152.4 | 233.7 |

**Table 2.** Age, weight and height of patients.

| Serological Markers | Percentage |
|---|---|
| % RF Positive | 40.0% |
| % RF Negative | 48.0% |
| % RF Not Available | 12.0% |
| **Serological Markers** | **Mean (SD)** |
| ESR (mm/h) | 23.02 (17.60) |
| CRP (mg/L) | 10.12 (24.39) |

**Table 3.** Serological markers of patients.
ESR = Erythrocyte sedimentation rate,
CRP = C-reactive protein,
RF = Rheumatoid Factor, RF negative <20 µL/mL,

| Pharmaceuticals | Percentage |
|---|---|
| % on NSAIDs | 72.0% |
| % Not on NSAIDs | 26.0% |
| % Not Sure if on NSAIDs | 2.0% |
| % on MTX | 90.0% |
| % Not on MTX | 8.0% |
| % Not Sure if on MTX | 2.0% |

**Table 4.** Pharmaceutical data of patients.
NSAIDS = Non-steroidal anti-inflammatory drugs,
MTX = Methotrexate

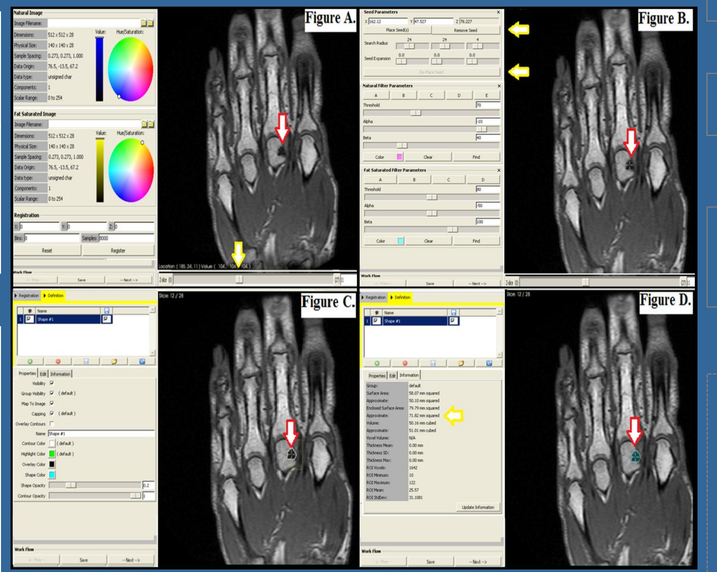


**Figure 3.** Readers opened the MR image on the EERA software and manually chose the image slide for seeding. (Figure A). Readers placed the seed point near the middle of the erosion and then automatically re-run the seeding until stabilization is achieved (Figure B). Readers manually chose from one of the five potential software parameters labeled A to E that best fits the contours of the bone erosion (Figure C). The EERA software then generates a total volume score of the erosion (Figure D).

## RESULTS

Of the 50 participants recruited for the study, 16 were males and 34 were females. Study subjects had a mean age of 57 (SD=11.5), a mean weight of 78 kg (SD=15.6), and a mean height of 169 cm (SD=13.9) (See Table 2. Patient Demographics). Readers identified 64 ± 1 erosions in the patients: 15 of these occurred in second MCP, 33 ± 1 occurred on the third MCP, 12 ± 1 occurred in the fourth MCP, and 4 occurred in the fifth MCP. The mean erosion size as determined by R1 during the first and second runs were 87.9mm$^3$ (SD=118.9) and 88.1mm$^3$ (SD=121.2) respectively. R2's measures had a mean erosion volume of 90.7mm$^3$ (SD=130.1) for the first run and 103.2mm$^3$ (SD=151.0) for the second run.

For both runs, agreement between readers was better for smaller sized erosions decreasing appreciably beyond 100mm$^3$ (See Figure 1. and Figure 2.). The intra-rater reliability had an ICC value of 0.956 with the 95% confidence interval ranging from 0.935 to 0.970. Between R1 and R2, the inter-rater reliability had an ICC value of 0.921 with a 95% confidence interval from 0.886 to 0.946.

## CONCLUSION

Results obtained suggest that EERA software can be applied to acquire MCP erosion volume measures in a reliable manner.

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