

Targeted *In Vivo* Measurements of Small Cartilage Defect Volumes in Knee Joint MR Images

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Introduction

There is increasing need for non-invasive imaging tools capable of detecting and evaluating cartilage defects as well as for monitoring response to new cartilage repair therapies. Of all techniques, Magnetic resonance imaging (MRI) has shown the greatest promise motivating studies to determine whether it is accurate and reproducible enough to quantitatively measure the volume and thickness of cartilage tissue. Most work to date has focused on measurements of large cartilage volumes on *in-vitro* specimens without the effect of inter-scan or intra- and inter-operator variability. Because of clinical importance of these later effects, this study quantitatively assessed the *in vivo* reproducibility of small and clinically relevant (up to 12.7mm diameter) cartilage defect measurements from MRI of the knee using image processing tools.

Materials and Methods

Data Acquisition

We acquired baseline and short-term follow up MRI scans of the knee in the sagittal and coronal planes from eight patients with clinical indication of osteoarthritis in the knee. The two separate MRI scans were from the same knee and were performed at an average interval of 10 days from each other. All MR imaging was performed on a whole body magnet operating at a field strength of 1.5T (GE Signa). Pulse sequences routinely used for knee MRI scans were used. Specifically, a rapid scout scan was acquired in the axial, coronal and sagittal planes using a gradient echo sequence to make sure of the proper positioning of the knee, followed by three-dimensional spoiled gradient-echo (3D SPGR) sequences in the sagittal and coronal planes. A total of 64 3D SPGR images were acquired for each view (i.e. sagittal, coronal). The images were 256 by 256 pixels in size at 0.55 mm by 0.55 mm pixel resolution and 1.5 mm slice image spacing.

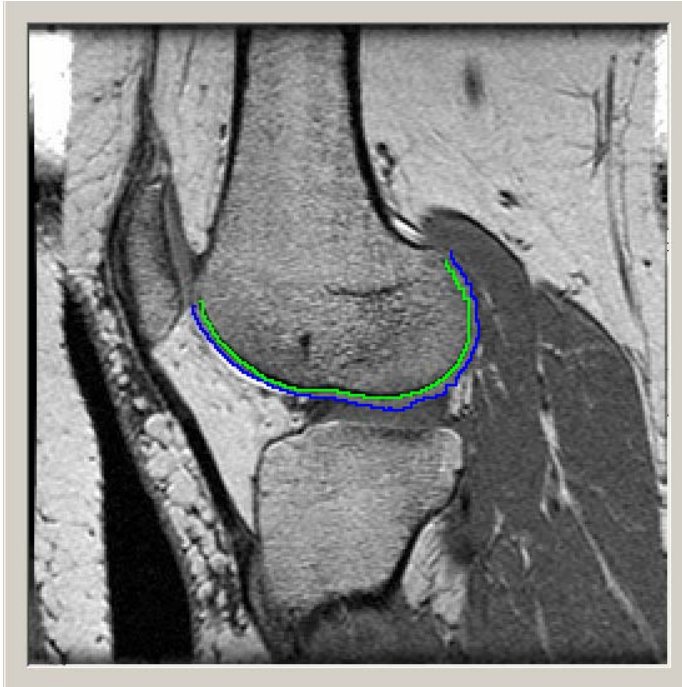


Figure 1. Illustration of the segmentation of the femoral cartilage tissue from a sagittal slice image.

Image Segmentation

The femoral cartilage boundaries from the MR image scans were identified using a Live-Wire based segmentation tool developed at Imaging Therapeutics (ImaTx) (Figure 1). Since the segmentation requires user interaction and thus some familiarity with the use of the image processing tools and the task at hand, three operators with low, average and high skill levels segmented the cartilage regions from the MR images.

Targeted Cartilage Defect Simulation

Cartilage defects were simulated as cylindrical volumes of three different radii: $\frac{1}{4}$ ", $\frac{3}{8}$ " and $\frac{1}{2}$ ", and height corresponding to the cartilage thickness. Several defects were extracted randomly without overlap from each baseline segmented image (Figure 2). Segmented surface points were selected as part of a defect based on a random center point and a defect radius (Figure 3).

Each defect volume was measured based only on the points from the corresponding segmented bone and cartilage surfaces contained within the cylindrical volume shape used to select them. The distances between points and corresponding pixel and slice thickness resolutions were used for calculating volume measurements relating to the actual MRI resolution. The volume measurement error associated with this approach can be approximated as $\pm\pi r(r+h)\Delta/2$ where r is the corresponding cylinder radius; h is the average height or cartilage thickness and Δ is the average isotropic voxel resolution ($\Delta=0.873\text{mm}$). Considering an average cartilage thickness of $h=3\text{mm}$, the ranges for this measurement error are $\pm 18.6\text{mm}^3$, $\pm 37.25\text{mm}^3$ and $\pm 52.4\text{mm}^3$ for defect diameters of 6.35mm ($\frac{1}{4}$ "), 9.52mm ($\frac{3}{8}$ ") and 12.7mm ($\frac{1}{2}$ ") respectively and corresponding average volumes of 95mm^3 , 213.5mm^3 and 380mm^3 . The associated 95% confidence interval for differentiating the three average volumes is $\pm 59\text{mm}^3$.

Reproducibility Analysis

Intra- and inter-observer reproducibility. Each one of the three observers segmented the femoral cartilage boundary surfaces from a subset of the patient knee scans and then repeated the segmentations. Each observer performed the segmentations over the span of at least a couple of weeks. The order in which the knee scans were segmented between repetitions was modified in order to minimize memory biases and broaden the factors influencing observer variability. Focal cartilage volumes simulated and measured from the initial segmentations were then compared to volumes extracted from repetition segmentation sets of the corresponding knee performed either by the same observer (for intra-observer variability) or one of the other two observers in the panel (for inter-observer variability). The analysis and comparison of each estimated volume set for reproducibility was performed using linear regression and the associated R^2 and p -value parameters. For system variability evaluation, the average percent error was estimated for each observer and comparison scenario.

Inter-scan reproducibility. Focal volumes simulated and measured from each baseline MRI scan segmentation set were compared to the corresponding volumes extracted from segmentations of corresponding follow-up scans. The correspondence of volumes from baseline scans to the measured values based on follow-up scans was evaluated through linear regression and the associated R^2 and p -value parameters. The average percent error was also estimated for estimation of system variability.

Image Registration

The position of a knee in an MRI scanner changes for scans taken at separate times and after the patient moves in and out of the scanner. Because of this, one data set has to be transformed in such a way so that the structures in both data sets are aligned (or registered) with each other. We aligned the baseline and follow-up datasets by registering the segmented bone surface in one set with the bone surface in the other data set using software developed at ImaTx for non-elastic surface registration. Figure 4 shows an example of a baseline and a follow-up scans before and after the registration procedure. An example of the distance map between registered scans is shown in Figure 5.

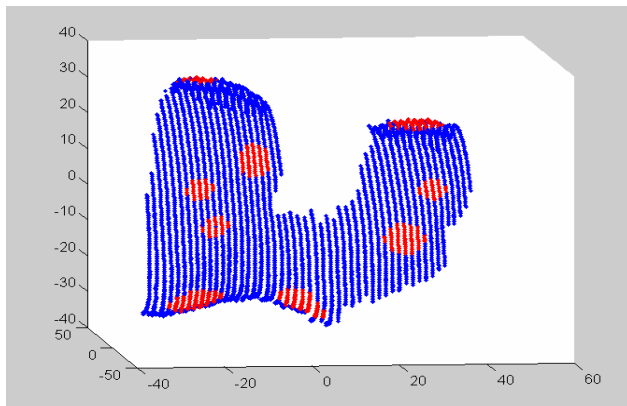


Figure 2. Example illustrating the random placement of the focal cartilage defects on a segmented femoral bone-cartilage surface.

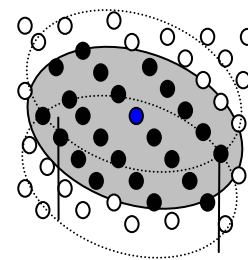


Figure 3. Cylindrical shape and random center point defining which segmented bone surface points are selected for focal defect.

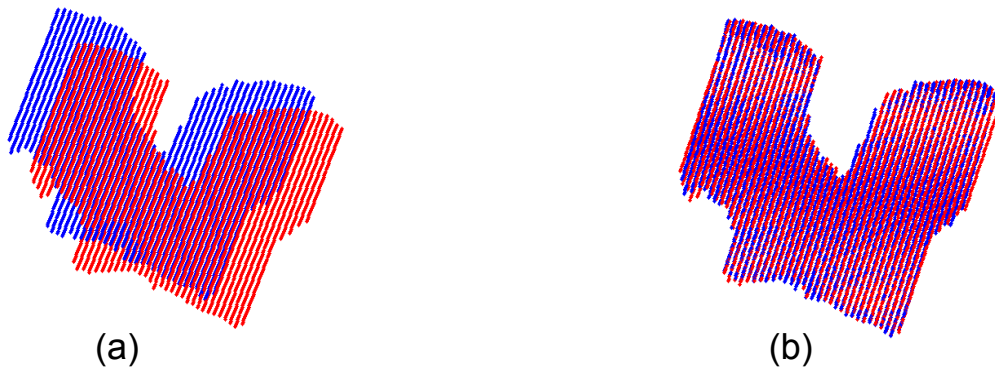


Figure 4. Example of baseline and follow-up segmented scans before (a) and after registration (b).

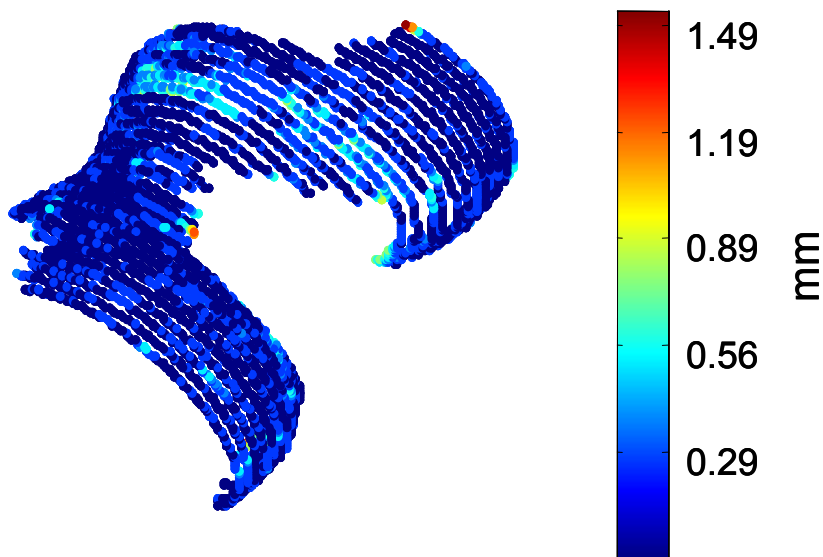


Figure 5. Example point to point minimum distance between registered scans. The distance associated with each point is shown relative to a colormap.

Results

The results summarized in Figures 6 through 7 and Tables 1 through 2 show the intra- and inter-observer system reproducibility and variability. The inter-scan test results are summarized in Figure 8 and Table 3.

Intra- and inter-observer reproducibility showed consistent improvement with increased operator skill (R^2 (low) =0.95, R^2 (high) =0.99, average R^2 =0.96). For inter-scan reproducibility, results with 270 focal cartilage defect measurements show high measurement correlation (average R^2 of 0.95) between baseline and follow up scans.

Table 1. Intra-observer variability. Average volume difference and percent error between same scan volume comparisons for all observers.

Defect diameter	# Defects generated	Average volume difference ¹ (\pm mm ³)	Average percent error ²
All	396	12.9925	5.5255
1/4"	132	5.4606	5.9702
3/8"	132	13.2860	5.8263
1/2"	132	20.2311	4.7800

Table 2. Inter-observer variability. Average volume difference and percent error between same scan volume comparisons for all inter-observer combinations.

Defect diameter	# Defects generated	Average volume difference ¹ (\pm mm ³)	Average percent error ²
All	288	13.2277	6.0192
1/4"	96	5.6842	6.4745
3/8"	96	16.8650	7.3134
1/2"	96	17.1339	4.2698

Table 3. Inter-scan variability. Average volume difference and percent error between baseline and follow-up scans: all combined observers.

Defect diameter	# Defects generated	Average volume difference ¹ (\pm mm ³)	Average percent error ²
All	414	22.0827	9.19
1/4"	138	9.4089	9.54
3/8"	138	22.7636	9.78
1/2"	138	34.0757	8.24

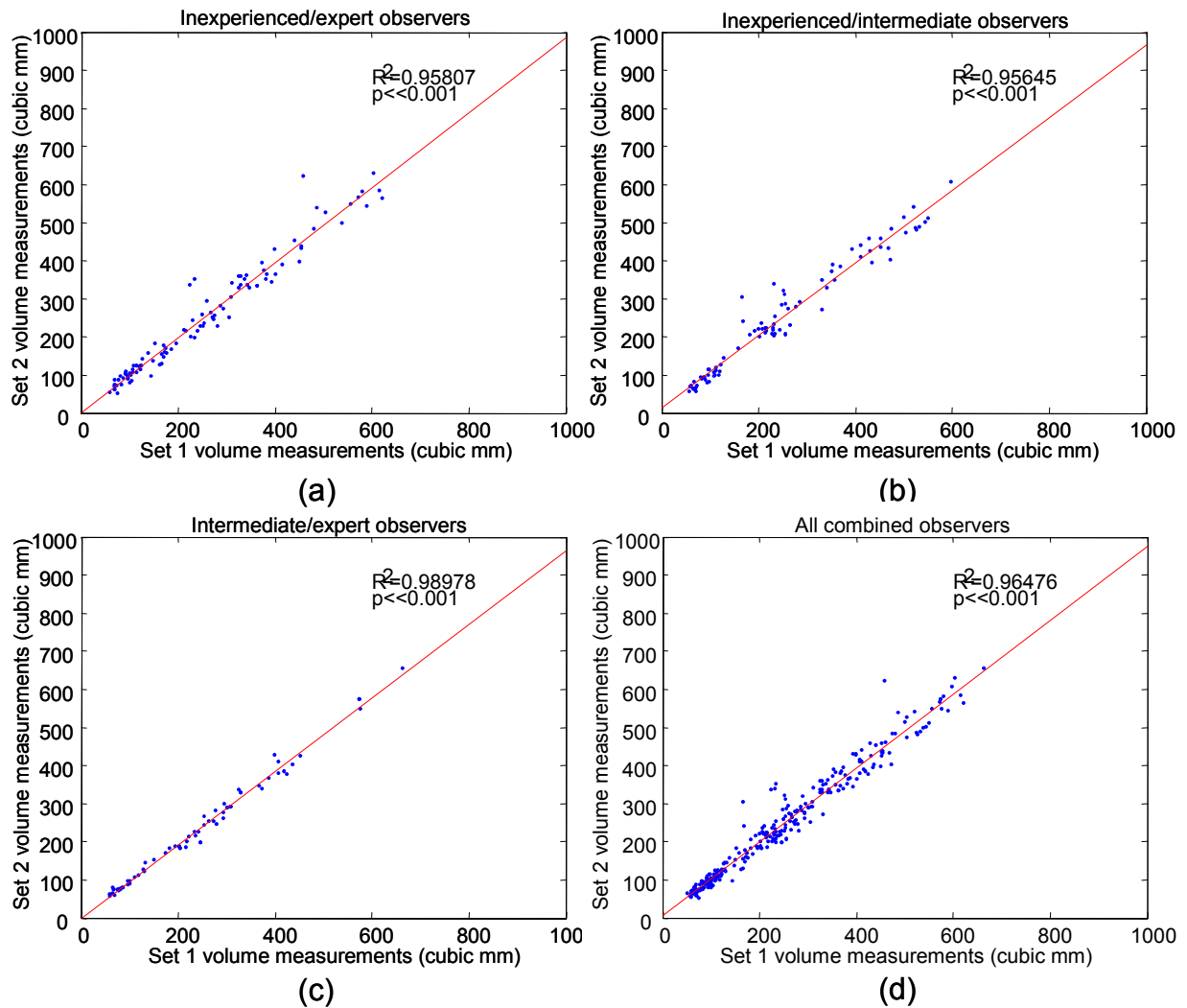


Figure 7. Inter-observer reproducibility. Linear regression fits between same-scan volume measurements: Inexperienced-experienced observer (a), inexperienced-intermediate observer (b), intermediate-expert observer (c) and all combined inter-comparisons (d).

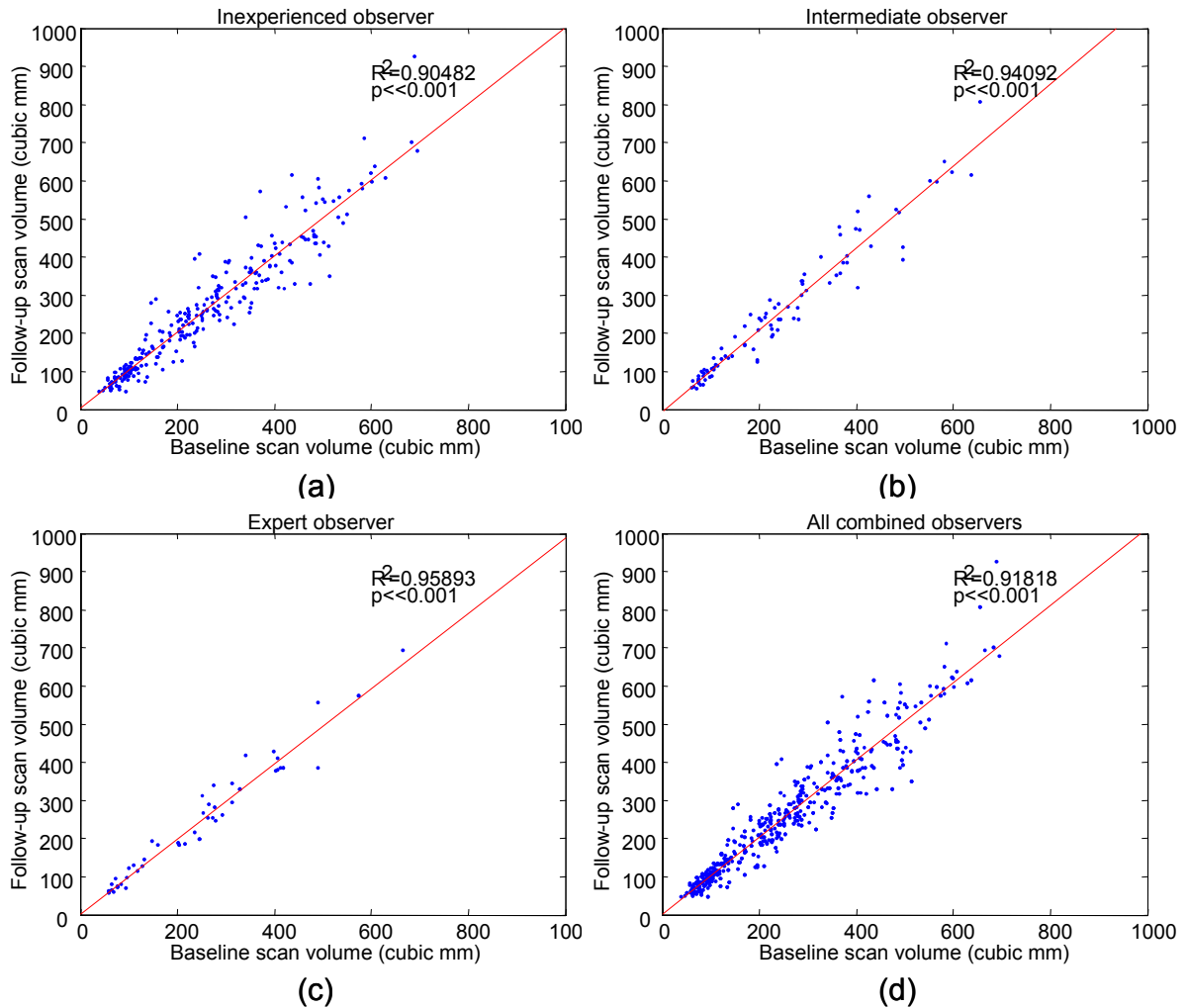


Figure 8. Inter-scan reproducibility. Linear regression fits between baseline and follow-up scans: inexperienced observer (a), intermediate observer (b), experienced observer (c) and all observers combined (d).

Conclusions

We were able to quantitatively and reproducibly measure targeted small cartilage defect volumes from *in-vivo* MRIs. Results show very high correlations between repeated measurements implying strong reproducibility on volume measurement performance. Intra and inter observer reproducibility can be optimized and variability minimized by either increasing operator skill level or improving the automation of the segmentation process. The possibility for improving inter-scan reproducibility with higher MR scan resolution and 3D image processing algorithms further emphasizes the potential usefulness of MRI as a non-invasive tool for *in-vivo* quantitative assessment of cartilage disease, disease progression, and monitoring response to treatment.