

Longitudinal measurements of signal intensity as a potential marker for cartilage degeneration in osteoarthritis

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Introduction

Recent studies have cast doubt on the effectiveness of total cartilage volume as a measure of cartilage degeneration in OA [1] and suggest that future work should concentrate on assessing focal changes e.g. by mapping cartilage thickness. In addition, a number of techniques exist to investigate the compositional integrity of cartilage such as proton density measurement and T2 mapping to probe water content, dGEMRIC to probe proteoglycan content and magnetisation transfer to probe collagen structure [2]. In the present study we have investigated the usefulness of signal intensity as a marker for disease progression in OA. The advantage of a signal intensity measurement is that, unlike other measurements of cartilage quality, it can be obtained from the structural scans so that no additional scan time is required.

Methods

The aim is to compare signal intensity in 3D gradient echo images produced for the same individual at different times. In order to compare corresponding locations within the cartilage, we first register the images. An overall rigid registration is not possible because the relative positions of the components of the knee joint can change, but a separate rigid registration from each cartilage compartment (femoral, patellar, tibial) is a good approximation. This is achieved by constructing a triangulated surface (see fig 1) from manual segmentation of the baseline image, building a single example Active Appearance Model [3] using the surface and the image intensities and using the model to search the later time point images. This results in a translation and rotation for each compartment. The image intensity is sampled at a set of corresponding points in each of the images using linear interpolation. In initial experiments these points corresponded to the grid of voxel locations in the baseline image ('rigid sampling') but in more recent experiments we have developed a method to sample along normals to the medial surface of the triangulation ('thickness sampling'). The final step is to correct for an overall scaling factor caused by changes in scanner settings. This is achieved by performing a robust fit (least median orthogonal distance) of a pair of sets of corresponding signal intensities. Once the scaling factor is determined in this way, differences in signal intensity over time can be investigated.

The method was applied to two fat suppressed 3D gradient echo data sets. In the first, eleven patients with established OA of the knee were imaged at baseline, 2 months, 1 year and 3 years using a 1.0T clinical scanner (TR/TE=50/11ms, 40° flip angle, sagittal 1.56mm thick slices, 0.55mm in-plane resolution) [1]. In the second, 50 patients were imaged at baseline, 3 months, 6 months and 1 year (with some repeated measurements at 3 and 6 months) on a 1.5T scanner (TR/TE=58/6ms, 40° flip angle, sagittal 2mm thick slices, 0.63mm in-plane resolution). In both these data sets measurements of per compartment total cartilage volume yielded no significant change over the timescales of the studies.

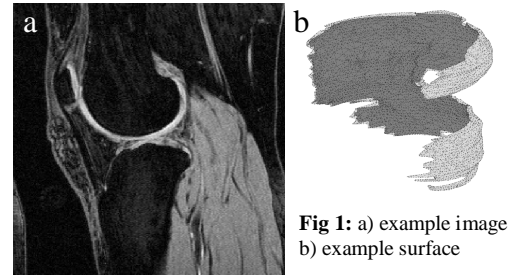


Fig 1: a) example image
b) example surface

Results and discussion

In fig 2 we present example results for a single slice through the cartilage. These images demonstrate the effectiveness of the registration process and allow local comparisons of signal intensity and so cartilage quality to be made. Some focal changes can be seen in the tibial plateau in this example (arrow fig 2).

The normalisation method we have used does not completely balance the mean signal intensity differences. The remaining global change in intensity tells us about changes in the outliers of the distribution. These will include voxels subject to varying degrees of partial volume averaging but will also include those voxels for which a real change in signal intensity has occurred. Differences in signal intensity due to e.g. partial volume changes or differences in position in the coil will vary randomly over time whereas real differences in cartilage composition will change in some consistent way. Average net changes have been calculated by linear regression of the average normalised signal intensity against time for the separate cartilage compartments. For the 11 patients over 3 years two data sets could not be used because of problems with the images at one of the time points. For the 9 complete sets we obtain results using rigid sampling, expressed as average % change per year (mean±standard error), femoral: -0.41 ± 0.19 ($P=0.07$); patellar: -0.92 ± 0.78 ($P=0.3$); lateral tibial: -0.22 ± 0.10 ($P=0.06$); medial tibial: -0.65 ± 0.34 ($P=0.09$). The probabilities quoted are for a two-tailed Student's t-test. For all four compartments there is a mean decrease in overall signal intensity but in no single compartment does this reach statistical significance at a 5% level, perhaps due to the small number of individuals in this study. The standard error is much larger in the case of the patellar cartilage than the other compartments; this is probably due to a combination of the increased error in registration because of the shape of this compartment and the fact that the patellar tends to sit near the edge of the knee coil where the receive sensitivity is less homogeneous. In the larger data set of 50 patients over one year we have 42 complete data sets that we have analysed using thickness sampling. The results for the femoral compartment show an annual decrease in signal intensity of -1.02 ± 0.29 ($P<0.01$) and in this case the result is significant statistically. We have also performed a reverse experiment (28 subjects) in which we use the last time point image as the baseline and find that the results are consistent at -1.15 ± 0.39 .

In conclusion, local signal intensity appears to offer important additional information in a study of cartilage quantity. The signal intensity in a gradient echo image is proportional to proton density (and hence cartilage hydration) but is also affected by T_1 and T_2^* , both of which may change with cartilage degeneration. It is therefore a non-specific marker for changes in cartilage composition but nevertheless should prove useful particularly if combined with studies of regional cartilage thickness.

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References

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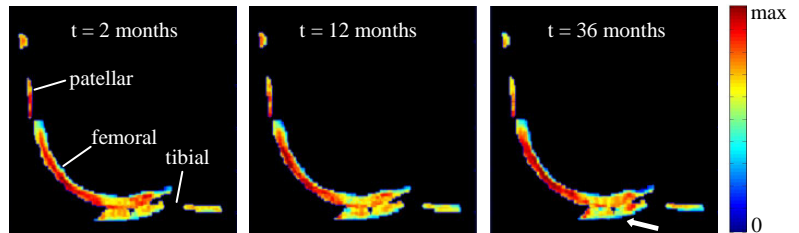


Fig 2: slice through registered and normalised cartilage compartments for three time points