Author's response to reviews

Title: Optimal Sampling Of MRI Slices For The Assessment Of Knee Cartilage Volume For Cross-Sectional And Longitudinal Studies

Authors:

Guangju Zhai (gzhai@utas.edu.au)  Changhui Ding (Changhai.Ding@utas.edu.au)  Flavia M. Cicuttini (Flavia.Cicuttini@med.monash.edu.au)  Graeme Jones (g.jones@utas.edu.au)

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Author’s response to reviews:

17 December 2004

To the Editor, BMC Musculoskeletal Disorders

Dear Sir/Madam

Re: MS: 1252540291464332

The Optimal Slice Thickness Of MRI Scans For The Assessment Of Knee Cartilage Volume For Cross-Sectional And Longitudinal Studies

the revised title: Optimal Sampling Of MRI Slices For The Assessment Of Knee Cartilage Volume For Cross-Sectional And Longitudinal Studies

Thank you for your email of 3rd December. We thank the reviewers for their comments. We have carefully considered their comments and have revised the manuscript accordingly as outlined on the responses to the comments. Changes on the manuscript are marked in bold and the line numbers are displayed on the margin of each page for your convenience. I confirm that this revision has been read and approved by all co-authors.

My co-authors and I look forward to hearing from you.

Yours sincerely

Guangju Zhai

Menzies Research Institute

Private Bag 23, Hobart, Tasmania 7001

Australia

Tel: +61 3 6226 7769
Responses to the comments

To reviewer 1 Stephen Gandy

Major compulsory revisions

1. Definition of slice thickness

Volume measurements for the ‘3mm’, ‘4.5mm’, and ‘6mm’ image slices have actually been extracted from the original 1.5mm slice thickness acquisitions. These images do not therefore contain the cartilage partial volume errors that real 3mm, 4.5mm or 6mm slices would demonstrate. Analysis of one in every two, three or four thin image slices in fundamentally not the same as analysis of one image slice that is two, three or four times thicker than the original.

We thank the reviewer for pointing this out. What we demonstrated in this study was that selective sampling of 1.5 mm thick slices of MRI scan will decrease post scan processing time for the assessment of knee cartilage volume for cross-sectional and longitudinal studies. We have now clarified this throughout the manuscript including the title. (See the revision, changes are marked in bold throughout the manuscript and the line numbers are displayed on the margin of each page).

If the described methods are implemented, then post-processing time could well be reduced substantially (e.g. by analysing every two, three or four slices - as described), but a reduction in the scan time (presumably by using thicker slices) really cannot be justified from these data.

We agree that a reduction in the scan time cannot be justified from this data, as the scan time is now only 6 minutes. We now restate our conclusion more explicitly. See Background and conclusion sections in abstract, page 3 lines 16-24 and the last paragraph on page 12.

Minimisation of partial volume errors is particularly important for patients with knee osteoarthritis, since the disease is often focal in the cartilage and could easily be missed (on a per patient basis) if slices are either too thick or are overlooked.

We agree that OA can be focal. However, previous publications from our institution (ref 25) show a global reduction in cartilage volume with OA. To assess focal disease we have also been measuring cartilage defects but that is not the point of this manuscript. We now state this as a limitation (page 11, lines 9-13)

2. Lack of femoral cartilage volumes

I was surprised to read that femoral cartilage volumes were not analysed as part of this study. Femoral cartilage is centrally involved in both patellofemoral and tibiofemoral joint osteoarthritis, and should not be ignored. From personal experience I am aware that the partial volumes that arise when segmenting sagittal femoral cartilage images are rather acute (much more so than for the other compartments included in this report). This is particularly evident when slices close to the inner and outer edges of the medial and lateral condyles are considered. It would be interesting and important to see what effect the authors’ selective slice analysis technique would have on cross-sectional and longitudinal femoral cartilage volume measurements, and also what effect true 3mm, 4.5mm and 6mm slices would have on the measured volumes in all compartments. If these data are available, or will soon be available, then they should be included.
There are a number of reasons why we do not include femoral cartilage volume which have been outlined in previous reports from our group but we have now restated in the methods section of this paper (see page 5 lines 14-18):

a. Femoral cartilage volume is strongly correlated with tibial cartilage volume and thus adds little extra information;

b. Tibial cartilage volume is the parameter that is most frequently examined in the literature;

c. Measuring femoral cartilage volume takes a much longer time than tibial cartilage volume, which makes large-scale studies very difficult (usually 1.5 hours per person by our method) and has worse reproducibility (4.5 v 2-2.5%).

Minor Essential Revisions:

1. Quality Assurance Validation of MRI Slice Thickness

Since slice thickness is the main focus of this paper, have the authors performed any Quality Assurance on their scanner to verify that the slice thickness that they have used is actually 1.5 mm? There is usually a fair degree of error associated with slice thickness measurements, with the values often being over-estimated e.g. a sequence with an 'apparent' 1.5 mm slice thickness may actually be delivering a slice thickness nearer to 2.0 mm in practice). The true value of the slice thicknesses used in this paper would probably not affect the presented results significantly, but a mention of a Quality Assurance Strategy would give readers added confidence in the reported data should they wish to undertake similar studies.

Yes, Philips Quality Procedure was used to assure our 1.5 mm thick slice is 1.5 +/- 0.1mm thick slice. See page 4 lines 18-19.

2. Difference In Lateral /Medial Tibial Cartilage Volumes In Tasoac V Kcv Cohorts

It seems counter intuitive that the older TASOAC cohort with higher recorded ROA have larger lateral and medial tibial cartilage volumes than those younger patients in the KCV study with less ROA? Is there any reason for this? One might have expected this volume difference to be the other way around, bearing in mind the authors' earlier publication documenting 5% loss of knee cartilage per annum in OA patients.

We agree that the TASOAC cohort having higher cartilage volume than the younger KCV cohort is surprising. In another report, there is no association between age and cartilage volume (G Jones, ARD, in press) so this may be real. However, this is not an issue in the current study as it is a method comparison study and doesn't include the full sample from each study (N=1370).

3. Potential Validity For Longitudinal Studies

One of the points raised in the discussion considers the potential importance of different observers and MRI machines being used to acquire and analyse MRI knee cartilage volume data for longitudinal studies. I was not completely clear whether all of the data from the patients in these two cohorts (ASOA and KCV) had been acquired from the same Picker MRI scanner described in the methods? Is it possible that there might be some sort of error(random or systematic) that could explain the volume differences discussed in 4, above? It would be useful for this to be clarified more clearly in the manuscript.

Yes, all the data for all participants (TASOAC and KCV, cross-sectional and longitudinal) was acquired from the same machine using the same protocol. We now state this clearly (page 4 lines 17-18).
4. List of References

The reference list has neglected some rather significant work in the field of MRI knee cartilage volume imaging. It is clear that the authors have published substantially in this area, but currently over 50% of the MRI knee cartilage volume references listed in this manuscript are 'in house'. Significant contributions to this field have been published by other groups e.g Eckstei/Reiser et al from Munich, Germany, Peterfy/Genant et al from UCSF, USA, and Waterton et al from Manchester, UK. These publications have covered topics such as validation of MRI knee cartilage acquisition methods, slice orientations, volume analysis methodology, intra-/interobserver CoV analysis, longitudinal changes (daily, yearly, short term response to exercise etc). It would be beneficial to widen the scope of the references where possible to aid the interested reader.

We have now broadened the references (see references).

5. Page 6 - final sentence of 'Other Measurements' paragraph - the total score of knee ROA could vary from 0-12. Further down in the Results section and in table 1, the total ROA score seems to be defined as having a maximum score of 9. This should be standardised, maximum either 9 or 12, or the difference in each scoring system explained more clearly.

We now correct this (page 7 line 6 and table 1).

6. Page 9 - the 9% discrepancy between cartilage volume and water displacement: - similar data have also been published by other groups, and should be included here.

We now include others in the references (see page 9 lines 19).

To reviewer 2 Lyn March

Minor Essential Revisions:

Page 6 mentions ROA as max 12 in first line and then talks of 3 our of 9 in last line.

We now correct this (page 7 line 6 and table 1).

Discretionary Revisions:

1. They have only addressed cartilage volume and no other aspects of knee structure such as cartilage defects/quality and subchondral bone which are of growing importance in OA research. This should be addressed in discussion or included in the results if they have analysed it.

Post-processing time for cartilage defects (average 20 minutes for the whole knee joint) and subchondral bone area (maximum three slices need to be measured) or bone marrow lesions (average 15 minutes for the whole joint) is much less than for cartilage volume, therefore using the whole sample of 1.5mm slices is much less of a problem for these other parameters. We have made no changes.
2. The authors do state that the patients in both groups had at best mild radiographic OA. The trend was evident for differences between the slice thicknesses to be greater in the presence of ROA. The authors should acknowledge this as a potential limitation and that it may not be generalisable to more advanced OA where greater irregularities and heterogeneity in cartilage thickness are evident.

We now include this as a potential limitation in the discussion (page 12 lines 1-2).