Author's response to reviews

Title: Size and Position of the Healthy Meniscus, and its Correlation with Sex, Height, Weight, Bone Size, and Age - a cross-sectional study

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Author's response to reviews: see over
Itemized revision letter MS: 4857847775315244
Size and Position of the Healthy Meniscus, and its Correlation with Sex, Height, Weight, Bone Size, and Age - a cross-sectional study
Katja Bloecker, Martin Englund, Wolfgang Wirth, Martin Hudelmaier, Rainer Burgkart, Richard Frobell and Felix Eckstein

Editorial comments:

Author comment and action: Thank you for giving us the opportunity to submit a revised version of the above manuscript.

We apologize for the delay, but based on the reviewer comments, new readings had to be made, which delayed completion of the revision.

We recommend that you copyedit the paper to improve the style of written English.

Author comment and action: We have carefully proofread the paper and asked a native speaker to double check the wording. We hope you find it improved.

We would be grateful if you could address the comments in a revised manuscript and provide a cover letter giving a point-by-point response to the concerns.

Author comment and action: Please find our itemized response to each reviewer concern below.

Please also highlight (with 'tracked changes'/coloured/underlines/highlighted text) all changes made when revising the manuscript to make it easier for the Editors to give you a prompt decision on your manuscript.

Author comment and action: We are submitting the revised manuscript with a track change and in a clean version, so that the changes are visible to the reviewer.

Please also ensure that your revised manuscript conforms to the journal style (http://www.biomedcentral.com/info/ifora/medicine_journals ). It is important that your files are correctly formatted.

Author comment and action: We have checked the consistency with the formal requirements.
Reviewer #1

Major Compulsory Revisions:
- Adjust for features that may be related to knee pain and meniscal position
- Assess the knee as whole organ to make sure they are healthy
- Assess meniscal tear/

Overall comments: The authors studied the size and position of the healthy menisci and their correlation with gender, height, weight, bone size and age, using the data from OAI. It is a well-written manuscript. A major limitation of this study is the fact the authors failed to fully make use of strength of MRI, i.e. they should have assessed the whole knee of all subjects using MRI to ascertain that those subjects did indeed have 'normal knees' without any evidence of OA. Relying on clinical assessment and radiographs only is a suboptimal method to achieve this. Additionally, there are other shortcomings in this study, which makes it less meaningful scientifically. Overall, unfortunately, I do not think findings of this study provides any potential hints as to why women have a greater incidence of symptomatic knee OA than men. A major concern in this study that may explain symptoms is morphological tear/damage to the meniscus that was not reported neither adjusted for in this study and which can by itself explain pain in this cohort.

Specific points:

Dear Dr. Guermazi,
Thank you for your suggestions. We have now had a new author (reader) assess meniscal integrity (tears, maceration, destruction according to semiquantitative BLOKS) and have excluded knees (n=15) with meniscal tears from the comparison. The quantitative results now presented in the paper (n=102) are only on subjects without meniscal pathology.

Below we have outlined in detail how we have dealt with your suggestions, which we found to be very helpful in improving the clarity, quality and scientific quality of the study.

1. The subjects of this study were meant to be 'normal' persons without OA. They were, however, all middle aged to elderly, and did not include any younger persons. Since authors are trying to find measures (either absolute or relative) for completely normal menisci, I don’t think they have chosen the appropriate subjects. They should be young subjects without any clinical, radiographic or MR evidence of OA. The subjects they used may be asymptomatic but even then we cannot exclude the possibility that they have some MRI-evidence of early OA. Radiography, as is well known nowadays, fails to detect any early OA features, which can only be appreciated by MRI.

Author comment:
The primary objective of this study was not to provide “normal” values for persons without any structural knee changes, but to compare meniscus morphometry in a group of men and women, who are “clinically” normal (no pain, no radiographic changes, no risk factors of
The fact that they are older may be seen as a weakness, but also is a strength, because it makes the values more directly comparable with those obtained in knees with radiographic OA, who generally are from persons in this age range.

The subjects we had chosen were without any clinical or radiographic evidence of OA (and also did not have risk factors). However, we admit that we were not able to make sure they were without MR evidence of OA, and we agree that painless and radiographically normal knees not necessarily are entirely healthy at an MRI structural level (Englund et al. NEJM 2008).

Author action:
In view of your above comments, we have now asked an additional investigator (Martin Englund, Department of Orthopedics, Lund University, Lund, Sweden and Clinical Epidemiology Research & Training Unit, Boston University School of Medicine, Boston, MA, USA) to perform detailed meniscus readings and to become a co-author on this paper. We have now excluded all knees (n=15) with meniscal tear and only included those 102 knees in the analysis who had normal meniscal integrity on MRI.

In the abstract, at the end of the method section, we now state:
“Knees with MRI signs of meniscus lesions were excluded.”

The method section (page 6, line 11-20) has now been expanded to state:
Because asymptomatic participants without radiographic knee OA are known to commonly display meniscus damage [23], knees with meniscus lesions on MRI were excluded. To this end, one clinical investigator (M.E.) read all knee MR images for the presence of meniscus tears, or maceration/destruction semi-quantitatively using the BLOKS scoring system [24] on the intermediately-weighted sagittal and coronal turbo spin-echo (IWTSE) sequences. Knees (n=15) having meniscus lesions were excluded from the study. Consequently, 62 women (mean age 54 [range 46-69] years; body height 1.64± 0.06 m; weight 62.3±8.4kg; BMI 23.2±2.7kg/m²) and 40 men (57 [45-79] years; body height 1.74 ± 0.07 m; weight 79.2 ± 8.2 kg; BMI 26.1±2.9kg/m²) were included.

In the result section (and in the result section of the abstract), all results have now been changed to those from the 102 participants without meniscus lesions in the semi-quantitative scoring.

2. This study is trying to find something that is characteristic to subjects without any knee OA. That means, this study itself has nothing to do with OA. This is a study of purely anatomical and mechanical property of menisci in normal subjects. Thus, the subjects do not necessarily have to come from database related to OA. A better approach would be to recruit young healthy volunteers, who are much less likely to have any signs (clinical, radiographic, or MRI-detected) of OA, or malalignment of the knee. Do authors expect to find the same results if they employed such subjects?

Author comment: It is true that the study is NOT about knees with OA. Although the knees studied come from the OAI database, they come from the “non-exposed”, healthy
(asymptomatic) “reference” cohort (F1; n=122 subjects), which was deliberately included by the OAI to allow for comparisons between non-OA and OA knees. As outline above, inclusion of only young subjects has advantages (lesser likelihood of pre-radiographic lesions), but also limits the directly comparability with OA knees (which is not part of this study, but may be part of future studies). Given that we have now excluded participants with meniscal pathology, we feel that the age should not be a limitation, but rather a strength.

Author action: Knees (n=15) with MRI meniscus tears have been excluded (see above)

3. This study fails to address potential confounding factors, i.e. malalignment of the knee and MRI-detected cartilage loss and ligamentous lesions. Were all knees of neutral alignment? If so, please clearly state. If not, the analysis should take this factor into account. For cartilage loss, since MR images are available, it should have been assessed. Did all subjects in this study have completely normal cartilage status? If any subjects had any cartilage loss, those subjects should have been excluded from the study. Likewise, any asymptomatic ligamentous lesions (which can be detected by MRI) may potentially contribute to instability and hence altered mechanics of the knee joint. In this respect, any subjects with any MRI-detected signs of early OA should have been excluded to achieve the stated aim of this study.

Author comment: Because the subjects were asymptomatic, radiographically normal and had no history of trauma or another large series of OA risk factors, we feel the likelihood that a considerable number of them have malalignment, cartilage lesions, ligamentous lesions, or other biomechanically relevant alterations relatively small, particularly after excluding those with meniscus pathology.

No long limb X-rays were acquired and we did not score the knees for cartilage and ligamentous lesions. This is now mentioned as a limitation of the study (see below). As mentioned above, the primary goal was to compare meniscus morphometry in men and women who are asymptomatic and radiographically normal, but not necessarily 100% without any structural alterations of the joint.

Author action: We now mention on page 10, line 14-22 in the discussion: A limitation of the study is that, although knees with MRI signs of meniscus lesions were excluded, the cartilage or ligament status of the knees, the limb alignment, and the radiographic biomechanical appearance of the pelvis and hip joint were not examined. Therefore, we cannot exclude with certainty, that some participants had early cartilage or ligamentous changes or deviations from neutral alignment. …… However, the subjects were asymptomatic, radiographically normal, and had no trauma history or any other risk factors of OA, and had no meniscus lesions.

4. Authors assessed 'height' and 'weight' separately. I wonder why they did not assess the data with 'body mass index (BMI)'. Since virtually all OA studies use BMI to stratify or adjust their analyses, I believe this study should also do that. Assessing height and weight separately fails to consider the fact that some subjects can be tall and thin, or short but fat. In such cases, it is not the absolute weight or height that matters. It is the BMI.
Author comment and action: It is true that in OA, BMI is an important risk factor. However, the correlation analysis here has an entirely different purpose, that is to identify whether body height or weight (which both scale with size-related parameters, such as meniscus size) can be used to normalize meniscus measures, particularly when including both men and women in the same study. Because BMI is a ratio of weight and height, it only has a poor correlation with meniscus size (data not shown) and therefore BMI is not optimal for such a normalization procedure, which is shown to work best for ipsilateral tibial plateau area.

5. In figure 3, error bars overlap between men and women in all graphs. This means there is, in fact, no statistically meaningful difference between men and women. How exactly does this finding 'provide potential hints as to why women have a greater incidence of symptomatic knee OA than men', which is the conclusive statement of this study? I think these graphs can be removed without sacrificing the meaningful content of this manuscript.

Author comment: An overlap in error bars between groups was not unexpected, as body size also overlaps between men and women.
We feel that this graph is very important to visualize that the normalization is very effective in removing absolute size difference of the meniscus between men and women, once normalization to tibial plateau area is performed.
We therefore kindly request that the figure is maintained in the manuscript.

Author action: We have removed the conclusive statement that this may provide potential hints to why women develop knee OA more often than men from the conclusion (we still mention it in the discussion), as this is admittedly speculative:

Discussion on page 12, line 13-20: Given that meniscal extrusion is known to contribute to the development (and progression) of knee OA [10-16], the finding of greater “physiological” medial meniscus extrusion in healthy women compared with healthy men is interesting. Whether this contributes to women having at greater risk of developing symptomatic knee OA than men [1-3] remains to be established in long-term follow-up studies in participants with incident knee OA.

Conclusion of the abstract on page 2, line 23-25: “These data suggest that meniscus surface area strongly scales with (ipsilateral) tibial plateau area across both sexes, and that tibial coverage by the meniscus is similar between men and women”.

6. Authors found 'medial meniscal extrusion was greater in healthy women than in men.' This is a somewhat self-contradictory statement. Subjects with meniscal extrusion may be 'healthy' in global terms, but the knee is exhibiting a clear pathological process (even if it is asymptomatic, extruded menisci are NOT NORMAL.’ Why are these subjects included in this study? Should they not have been excluded?
Author comment: We are sorry for this misunderstanding. We did not mean to use the term “extrusion” as it is used clinically (i.e. = pathological), but as descriptor of the distance between the external margin of the meniscus and of the tibial plateau.

Author action: Throughout the manuscript, we now use the term “physiological” extrusion. In the method section on page 7, line 23- page 8, line 2, when the term is introduced, we now state:
“Further, we computed the mean (and maximal distance between the external margin of ACdAB and TA [17]. These measures were termed mean (Ex.Me) and maximal “physiological” external meniscal extrusion (Ex.Max). This terminology is not meant to refer to a pathological condition but to describe the position of the meniscus in asymptomatic volunteers, e.g. under “physiological” conditions.

7. Another issue is that the study completely fails to take into account the difference between men and women of the structure and mechanical property of the hip joint. Since men and women have differently-shaped pelvis, their mechanical property of the hip joint, and thence the knee joint, will likely to be different. However, anthropologic studies have shown some women have ‘male-like’ pelvic shape (and subsequently have difficulty with childbirth.) This study should have included pelvic X-ray to exclude women who have ‘male-like’ pelvis. Otherwise, one ends up analyzing women of various shapes of hip and thus (hips and) knees which are exposed to men-like pattern of mechanical stress.

Author comment: We intended to compare meniscus size and position in a representative group of asymptomatic and radiographically normal knees of men and women, but not necessarily in a subcohort with typically female biomechanics. However, we agree that this should be mentioned in the limitations of the study.

Author action: On page 10, line 18-20, we now state: .....Further, we cannot exclude that some women had “male-like-shaped” pelvices and thus biomechanical conditions that were more similar to men than those of other women......

8. Authors present so many numbers in the tables presented. However, these numbers virtually mean nothing unless readers are the specialists of their analytic technique and quantitative assessment. Especially, table 3 and 4 mean very little to general readers. For example, correlation between Th.Me and Mt.AcdAB is .32/.32, and that between Wid.Me and Mt.ACdAB is .29/.34. These numbers are not important, as long as authors state there were no statistically significant correlation between these features. Also, see table 4. The correlation between V and Body weight is .02/.25 and authors indicated .02 in bold character (meaning statistically significant.) However, if you look at other columns showing values of >.02, they can be statistically non-significant. Thus, slavishly presenting all these values can actually be confusing and does not facilitate readers to interpret the data appropriately. I suggest authors provide a descriptive explanation of only pertinent findings from these analyses, and remove tables 3 and 4.

Author comment: We feel that deleting Tables 3 and 4 would hold back interesting data for the interest specialist, and would require the inclusion of more numbers in the text, which would decrease the flow of reading. It is true that some correlation coefficients in men may
be greater than in women, whilst those in women may be significant and those in men not. This is because the level of significance is determined by both the strength of the correlation and the size of the group. Because there were more women (n=62) than men (n=40), lower correlation coefficients in women may be significant, whereas those in men may not. Still, we feel we need to report which coefficients are statistically significant and which ones are not for the sake of scientific accuracy. For readers without special interest in detailed meniscal morphometry, we have tried to capture the relevant observation in the text of the result section, at the beginning of the discussion, and in the conclusion.

9. Page 8, line 9. Authors state "We find that men have significantly greater (absolute) tibial and meniscus surface areas than women as well as meniscus thickness and volume." This is surely expected without performing this study. I’d be surprised if the finding was otherwise.

Author comment: We agree that this finding was expected. Clearly, the primary purpose of the paper was not to detect something totally unexpected, but to put quantitative numbers on meniscus size and position in asymptomatic men and women, to eventually allow for quantitative comparisons between OA and asymptomatic knees.

10. Page 9, line 3. I am somewhat puzzled by the authors statement "Another limitation of our study is that the MR images were acquired in a supine and not in a weight-bearing position...". Why should the authors acquire MR images in weight-bearing position? Since the aim of this study is to examine the normal knees, weight bearing should not make any difference. If meniscal extrusion occurs in a weight-bearing position, that knee is exhibiting a pathology, and should be excluded from the study anyway.

Author comment and action: We agree that this paragraph is not absolutely necessary and have thus deleted it.

11. Page 9, line 19. Authors state "The total surface area of the meniscus (TOT A) showed very high correlations with meniscus volume and a moderate to high correlation with meniscus thickness and therefore provides a good and representative measure of meniscus size." Is this really surprising? Sounds more like 'common sense' to me. Do you really need to perform as detailed quantitative analyses as these to reach a conclusion as simple as this?

Author comment: As outlined above, the primary purpose of the paper was not to detect something totally unexpected or surprising at an observational level, but to put quantitative numbers on meniscus size and position in asymptomatic men and women, to eventually allow for quantitative comparisons between OA and asymptomatic knees.

Still we feel it is important to have established quantitatively that the ratio between meniscus size (surface area) and tibial plateau area is similar in men and women, and that this “relative” measure can thus be used in the future to evaluate potential “meniscus hypertrophy” across mixed cohorts of men and women. Not having these data in hand, we
do not think that such a comparison could be made but analysis would have to be performed separately for men and women.

12. As a conclusive remark, authors state "Although tibial plateau coverage by the meniscus was similar in healthy men and women, medial meniscal extrusion was greater in women. This may provide potential clues as to why women are at greater risk of symptomatic knee OA than men." I have a serious problem with this statement. As I stated before, subjects showing meniscal extrusion are already showing early signs of OA. Did these subjects not have any MRI-detectable OA features? Readers do not know the answer to this question, because authors did not provide the data. If authors are search any potential clues as to why women are more likely to have symptomatic OA than men, they have to catch subjects before they had meniscal extrusion. Thus, I regret to say that findings of this study do not provide any clues as to why women are more likely to have symptomatic OA than men.

Author comment: We agree that this statement was rather speculative. As outline above, we have made the following changes:

Author action:

Throughout the manuscript, we now use the term "physiological” extrusion. Also, in the method section on page 7, line 23- page 8, line 2, when the term is introduced, we now state:
“Further, we computed the mean (and maximal distance between the external margin of ACdAB and TA [17]. These measures were termed mean (Ex.Me) and maximal “physiological” external meniscal extrusion (Ex.Max). This terminology is not meant to refer to a pathological condition but to describe the position of the meniscus in asymptomatic volunteers, e.g. under “physiological” conditions.

Discussion on page 12, line 13-20: Given that meniscal extrusion is known to contribute to the development (and progression) of knee OA [10-16], the finding of greater “physiological” medial meniscus extrusion in healthy women compared with healthy men is interesting. Whether this contributes to women having at greater risk of developing symptomatic knee OA than men [1-3] remains to be established in long-term follow-up studies in participants with incident knee OA.

Conclusion of the abstract on page 2, line 23-25: “These data suggest that meniscus surface area strongly scales with (ipsilateral) tibial plateau area across both sexes, and that tibial coverage by the meniscus is similar between men and women “.

13. A major and critical problem of this manuscript is that authors use the term 'healthy' without strictly defining what they mean. In fact, they should not use this term. They should categorically state that subjects are 'those without clinical or radiographic signs of OA'. As I stated before, no radiographic signs of OA does not exclude the presence of early OA features that are detectable by MRI. Such subjects may be 'healthy' without any systemic diseases, but those knees are certainly NOT healthy. Critically, radiography
does not visualize cartilage or meniscus. Unless authors ascertain by using MRI that subjects do have clean and normal cartilage and meniscus, the analyses presented in this manuscript do not make any scientific sense.

Author comment: We agree that the term “healthy” is not ideal and have removed it from the manuscript.

Author action:

- We have now added semi-quantitative readings of the meniscus and have, excluded knees with meniscus lesions (n=15).
- We have eliminated the term “healthy” throughout the manuscript and now strictly refer to “asymptomatic knees without radiographic signs of knee OA, or risk factors of knee OA”.

Reviewer’s report (#2)
Title: Size and Position of the Healthy Meniscus, and its Correlation with Sex, Height, Weight, Bone Size, and Age - a cross-sectional study
Version: 2 Date: 4 May 2011
Reviewer: Michel D. D Crema
Reviewer’s report:
This is a cross-sectional study aiming to correlate the size and position of the healthy meniscus with variables such as sex, height, weight, age, and bone size.

This is a well-written manuscript with detailed methodology and analyses.

Dear Dr. Crema, thank you very much for your favorable comment.

However, there are several issues which directly impact on the objective and nature of this study:

Below we have outlined in detail how we have dealt with your suggestions, which we found to be very helpful in improving the clarity of the manuscript.

- One of main limitations of this study is the fact that the authors "assume" that the menisci in subjects without clinical symptoms (from the healthy reference cohort of OAI)are "healthy". This assumption can not be made based on the reported prevalence in the literature of meniscal lesions in asymptomatic subjects without radiographic OA. Furthermore, the meniscal integrity was never assessed in this study, meaning that we don’t know whether meniscal tears are present in such "healthy" cohort. It is widely known that different types of meniscal tears are associated with meniscal extrusion. Thus, we can not be sure in the present study that extrusion detected (especially in women) was not related to a prevalent meniscal tear.
Author comment:
Although we agree in principle with the reviewer, we would like to stress that the primary objective of this study was not to provide "normal" values for persons without any structural knee changes, but to compare meniscus morphometry in a group of men and women, who are “clinically” normal (no pain, no radiographic changes, no risk factors of OA)(see title). The fact that they are older may be seen as a weakness, but also is a strength, because it makes the values more directly comparable with those obtained in knees with radiographic OA, who generally are from persons in this age range.

The subjects we had chosen were without any clinical or radiographic evidence of OA (and also did not have risk factors). However, we admit that we were not able to make sure they were without MR evidence of OA, and we agree that painless and radiographically normal knees not necessarily are entirely healthy at an MRI structural level (Englund et al. NEJM 2008).

Author action:
- In view of your above comments, we have now asked an additional investigator (Martin Englund, Department of Orthopedics, Lund University, Lund, Sweden and Clinical Epidemiology Research & Training Unit, Boston University School of Medicine, Boston, MA, USA) to perform detailed meniscus readings and to become a co-author on this paper.
- We have now excluded all knees with signs of meniscus degeneration and only included those in the analysis who had normal menisci in MRI:

Method section, page 6, line 11-20:
“Because asymptomatic participants without radiographic knee OA are known to commonly display meniscus damage [23], knees with meniscus lesions on MRI were excluded. To this end, one clinical investigator (M.E.) read all knee MR images for the presence of meniscus tears, or maceration/destruction semi-quantitatively using the BLOKS scoring system [24] on the intermediately-weighted sagittal and coronal turbo spin-echo (IWTSE) sequences. Knees (n=15) having meniscus lesions were excluded from the study. Consequently, 62 women (mean age 54 [range 46-69] years; body height 1.64±0.06 m; weight 62.3±8.4kg; BMI 23.2±2.7kg/m²) and 40 men (57 [45-79] years); body height 1.74 ± 0.07 m; weight 79.2 ± 8.2 kg; BMI 26.1±2.9kg/m²) were included.

- Under limitations, we now state on page 10, line 14-22: “A limitation of the study is that, although knees with MRI signs of meniscus lesions were excluded, the cartilage or ligament status of the knees, the limb alignment, and the radiographic biomechanical appearance of the pelvis and hip joint were not examined. Therefore, we cannot exclude with certainty, that some participants had early cartilage or ligamentous changes or deviations from neutral alignment. Further, we cannot exclude that some women had “male-like-shaped” pelvices and thus biomechanical conditions that were more similar to men than those of other women. However, all subjects were asymptomatic, radiographically normal, had no trauma history or any other risk factors of OA, and had no meniscus lesions.”

- Further, we have eliminated the term “healthy” throughout the manuscript and now strictly refer to “asymptomatic knees without radiographic signs of knee OA, or risk factors of knee OA”.
- The authors give a lot of credit to meniscal hypertrophy in OA. Meniscal maceration, meaning loss of meniscal substance is much more common than meniscal hypertrophy in knee OA, especially in advanced OA. Further, it is very common to find meniscal tears in conjunction with meniscal maceration. How this data will help the understanding of the natural history of OA if it never evaluated associated meniscal tears? Loss of meniscal integrity (tears) is just important as it is extrusion in the prediction of structural deterioration in knee OA.

Author comment: We mention meniscus hypertrophy, because there has been recent literature on it (see Jung et al, Ref No 19). This is of interest in context of this methodology, because quantitative measures of meniscus size can potentially provide objective measures of hypertrophy by comparing OA with non-OA knees.

However, we admit that this issue also is of potential interest in context of quantitatively measuring meniscus maceration.

Author action:
- In the introduction of the text (page 5, line 16-17), we now state: “Similar considerations apply to quantitative measures of meniscal maceration (i.e. loss of substance).”
- Also, throughout the discussion, we mention that a “relative” measure of size can be used to study either hypertrophy or substance loss of the meniscus quantitatively
- We also hope that exclusion of the 15 knees with meniscus tears has helped to improve the manuscript and analysis.

- Another important limitation (although acknowledged by the authors) to this study is the use of coronal imaging for meniscal segmentation. I don't think this is a minor limitation as discussed, since it does not allow proper segmentation of both anterior and posterior horns; in the lateral meniscus, this represents 2/3 of meniscal volume, and it is even more problematic for the medial meniscus, as the posterior horn is fairly larger than the anterior horn (anterior + posterior have maybe more than 2/3 of volume). How the authors expect to present normative data on meniscal volume without properly segmenting the anterior and posterior body?

Author comment: We agree with the reviewer that this is a limitation. We still feel, however, that this does not dramatically impact on the ability to explore size differences of meniscus size, as partial volume effects in the anterior and posterior horns would largely be expected to be similar in men and women.

Author action: We now state in the discussion section on page 10, line 22- page 11, line 2: “A further limitation of the study is the use of only coronal MR images, which are ideal for assessing the meniscal body (and external extrusion), but display partial volume effects in the anterior and posterior horns and thus cannot be used to evaluate anterior (or posterior) meniscus extrusion [35]. Meniscal surfaces and volumes might thus be somewhat larger than those reported here,
but this effect is likely similar in men and women, so that the comparison between men and women is likely not substantially affected."

- Since there is so much data supporting the role of meniscal integrity in load distribution and shock absorption in the tibiofemoral compartments, it does not make sense to evaluate meniscal volume and position without evaluating meniscal integrity; e.g. presence of meniscal tears.

Author comment and action: We agree. As outlined above, we have now excluded knees (n=15) with meniscus lesions visible on MRI. Results are presented only for the 102 knees without meniscus pathology.

Reviewer's report (#3)
Title: Size and Position of the Healthy Meniscus, and its Correlation with Sex, Height, Weight, Bone Size, and Age - a cross-sectional study
Version: 2 Date: 6 May 2011
Reviewer: Richard Souza

Reviewer's report:
Excellent manuscript. A very careful analysis of the meniscal properties was done and is very well written. I have no Major Compulsory Revisions.

Dear Dr. Souza,
Thank you very much for your kind comment. Below we have outlined in detail how we have dealt with your suggestions, which we found to be very helpful in improving the clarity of the manuscript.

VERY Minor Essential Revisions:

1) Abstract: Results, last sentence - It may be valuable to indicate that the medial meniscus extrusion is non-normalized, as given the sex differences noted previously, a normalization might be expected. I do realize that the females were greater than males, even without normalization, but given the previous finding, it may better just to clarify.

Author comment: It is true that the meniscus extrusion measure (in mm) is not normalized. These values are difficult to normalize, as they can be very close to zero. However, given the distance is larger in women (who have a smaller tibial plateau area), normalization likely would even result in larger differences. However, we think for the reason stated above, normalization for a measure close to zero is problematic. Further, we also provide a measure that does not need normalization, which is the % area of the meniscus extruding over the tibial surface:

Result section (page 9, line 14-19): "However, the meniscus surface not covering (i.e. extruding) the medial ACdAB (TA.uncovp) was significantly larger in women than in men.
(12.1% vs. 10.0%; Table 1), whereas laterally the values were not significantly different (p=0.24; 6.4% in men vs. 5.6% in women; Table 2). Also, the mean “physiological” extrusion distance of medial menisci (but not that of lateral menisci) was significantly greater in women (1.81±1.06mm) than in men (1.24±1.18mm; p=0.013; Table 1).”

We therefore hope that it is acceptable to the reviewer if we leave the statement as is. We feel introducing the term “non-normalized” at this location in the abstract would be rather confusing to the reader.

2) Materials and Methods: Page 5, line 3 - Please add units to BMI data.

Author comment and action: We have added the unit kg/m² to the BMI data. (page 6, line 18, 20)

3) Materials and Methods: Page 5, line 13 - Please write out ACdAB as is done in The list of abbreviations page. Without this detailed definition, it is hard for the reader to understand how ACdAB is somehow an abbreviation of tibial plateau area.

Author comment and action (page 7, line 2-3): We totally agree and for more clarity have added the definition of ACdAB to the text.

4) Discussion: Page 10, line 20 - change “relatively” to “relative”.

Author comment and action (page 13, line 5): We have changed the term relatively to relative in the text.