Reviewer’s report

Title: Evaluation of Zonal Diversity of Cartilage Degeneration and Necessity of Pre-contrast Measurements Using Radial dGEMRIC in Adults with Acetabular Dysplasia

Version: 1 Date: 15 April 2012

Reviewer: Bernd Bittersohl

Reviewer’s report:

Major Compulsory Revisions:

TITLE:
In the field of cartilage scientists, the term “zone” rather applies for various depth wise regions than for various joint areas. Therefore, the phrase “Evaluation of Zonal Diversity of Cartilage Degeneration…” is misleading.

ABSTRACT:
The term “zonal pattern of cartilage degeneration” may be misleading. Explain abbreviations before using them (dGEMRIC).
Further clarify your MRI protocol (T1 sequence, field strength) and statistical methodology.
(The word count for the abstract is sufficient [350 words]).
The conclusion “Radial dGEMRIC … is useful … particular for those in early stages of secondary OA” cannot be derived from this study that lacks validation (cartilage grading based on radiographic observations is fairly gross) and statistical power. Of note, “compared to the subgroup without OA, the subgroup with mild OA showed a pronounced but not significant decrease in T1Gd.”
“Showed” is not a scientific term.

INTRODUCTION:
3rd sentence, 2nd paragraph: provide a reference.
2nd paragraph, 4th and 5th sentence: this section should be revised because it implies an automatic radial MR reformatting process. Radial T1Gd reformats may be (manually) obtained from a three-dimensional dGEMRIC data set. However radial dGEMRIC does not generate radial reformatted slices....
2nd paragraph, 6th sentence: “… have been confirmed to be related to the patterns of cartilage damage found by intra-operative assessment in hips with femoroacetabular impingement (FAI)”. This study by Bittersohl et al. (Reference 13) did not involve intra-operative cartilage assessment.

METHODS:
Subjects:
One drawback of this prospective study is the relatively inhomogeneous study cohort (age range: 14 years – 54 years, inclusion of patients with bilateral hip dysplasia [n=14, 67%], LCE angle range: -17° – 23°) as this may implicate significant variable cofounding (i.e. age related primary OA, individual cartilage bio-structure). Please comment.

How many patients with hip (sub-)luxation were included? (LCE angles of -17°)
Please provide Sharp angle measurements.

Clinical and radiographic assessments:
To stratify or grade the severity of hip dysplasia by the LCE angle only, involves the risk that the femoral head under-coverage is underrepresented in particular at the anterior and posterior aspects. Was a false-profile view available that allows for the assessment of the ventral center-edge angle as a potential determinant of the anterior acetabular coverage? More details on hip morphology would be of interest to rule out further morphologic abnormalities of the acetabulum and / or femoral head that may be associated with hip dysplasia (acetabular retroversion, femoral torsion).

MRI protocols and measurements:
Please provide further details on the MRI protocol. Was T1 mapping performed only? Which dual-flip angle GRE sequence has been utilized? What was the imaging time for each sequence and the whole protocol? Of note, it should be clarified if B1 field inhomogeneity correction has been undertaken (Siversson et al.)

2nd paragraph: “Based on the clock-face orientation reported in the literature, we…” This information is impractical. The regional classification is accurately described in this section (anterior, anterosuperior ...).

2nd paragraph:
Be more specific on the correct placement of the ROIs squares within cartilage bounds. How can you place the ROI area in an irregular damaged cartilage? What was your anatomic / morphologic reference? How many ROIs had to be excluded due to severe cartilage damage and or loss (23% hips had Tönnis 2-3 changes!) that compromised T1 analyses?

2nd paragraph:
Be more specific on your intra- and inter-reader analyses. Which measurements were repeated? Does this include a repeat radial reformatting?

Statistical analyses:
Pearson correlation - analyses has been used in order to reveal any correlation between LCE angles and T1Gd values. Please comment on the variable (T1, LCE) distribution.
“Mean values and 95% confidence intervals (95% CI) of radial T1pre, T1Gd and #R1 were calculated for each subgroup and one-way ANOVA analyses were used to compare radial T1pre, T1Gd and #R1 among the 3 subgroups.” More details are needed. ANOVA was performed to reveal statistically significant differences in T1pre, T1Gd, and #R1 in various radiographic grades (3 subgroups) of hip OA. This involves multiple comparisons (n=3). How did the authors adjust for the inflated probability of a Type I error (the family wise-type I error rate increases as the number of post hoc comparison increases referred to as cumulative Type I error or alpha inflation)? What was the correction factor? What tests have been performed to warrant an approximately normal variable distribution and equal variable variance? Of note, ANOVA requires independent variables whereas two dysplastic hips in the same patient (67%) may not be treated as an independent sample. Therefore, it should be clarified if bilateral observations were included in the statistical analyses. If this is the case, the correlation between bilateral observations should be accounted for in the statistical analysis. I would recommend consulting a biostatistician for assistance with the statistical analysis as ANOVA may not be the appropriate approach in this specific study sample.

RESULTS:
Intra- and inter-observer reliability analyses:
1st sentence: “High intra-observer correlation was detected…. with mean differences of -3ms…. # assessment of mean differences between two readings is two-sided and, thus, requires absolute values. The same applies for the inter-observer reliability analysis.

Last sentence: This sentence is only repeating the results that have been already outlined in the previous section and, thus, this sentence may be deleted.

Radial distribution of dGEMRIC indices:
3rd paragraph: Using the lower limit of the normal range of T1Gd (480ms) in articular cartilage of the hip joint as the reference standard (REFERENCE: Kim et al.) ….

This approach should be reconsidered. Kim et al. have reported T1Gd values of the weight-bearing region of dysplastic hips. The authors of the current study, however, performed radial T1Gd assessment. With regard to differences in MRI technique (2D multi-slice fast-spin-echo with saturation recovery vs. 3D isotropic dual-flip angle GRE) and known alterations of T1Gd values in various hip regions (anterior vs. superior and posterior), using Kim et al.’s T1Gd values as reference is at least uncertain. Unfortunately, the present study did not include normal hips as control. However, normative T1Gd values in various radial reformats have been reported that may be more applicable for comparison.

Correlation analyses:
Last sentence: “T1Gd and #R1 appear to be equally effective for evaluating cartilage degeneration….” # This conclusion cannot be drawn from the results of
this study as no significant difference in radial T1Gd was detected in any of the sub-regions between subgroup I and II. In contrast, compared to the hips without OA, a significant increase in #R1 was observed in the superoanterior (p = 0.023) and superior (p = 0.046) sub-regions in hips with mild OA.

DISCUSSION:
In general, be more specific on what makes this study a sound addition to the scientific field of hip joint cartilage evaluation.

2nd paragraph: “However, the decrease of T1Gd value in the posterior sub-region in hips without OA … was neither mentioned…” # This is not correct. The T1Gd drop in the posterior regions is well known.

4th paragraph: Please clarify your statement “For those cases without radiographic OA, dGEMRIC seems unnecessary.”

Further limitations of this study:
1) grading of hip joint cartilage based on radiographic criteria (hip joint degeneration may be advanced by the time the diagnosis of OA is made based on plain radiography)
2) Inhomogeneous study group
3) Inclusion of patients with bilateral hip dysplasia
4) ROI analyses included acetabular and femoral cartilage as one entity and contrast agent containing joint fluid and effusion particularly in areas of severe cartilage degeneration may have under-estimated the T1Gd value within certain ROIs.
5) Although dGEMRIC is reported to be a sensitive means for assessing early cartilage changes, no significant differences were noted between subgroup I (Tönnis grade 0) and subgroup II (Tönnis grade 1). Please comment. Reasons?

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
I declare that I have no competing interests.