ments for all four time points. Each one of the five repeated measurement were then summarized with the trimmed average (Average of the three middle measurements). The trimmed average measurements were used to compute the standardized femur curvature, the standardized minimum contrast, and the standardized minimum of medial and lateral tibia-to-femur bone distance. Those measurements were used as surrogate measurements for bone shape, tissue inflammation and unloaded tibia-femoral joint distance. Those measurements then were used to compute a tree variable linear composite metric associated to the OA grade (biomarker00 data set) and to the WOMAC score of the right knee (Joint0x data set). The weights of the linear combination of three variables were selected in such a way to provide a strong association to the total WOMAC score and the OA Grade score. The qMRI composite index then was evaluated for responsiveness to time using a linear model.

**Results:** From 196 subjects included in data release 3.C.1, only 179 subjects had the complete set of four time points with full MRI quantification. The computed qMRI composite index was associated to total WOMAC ($r=0.33$, $t=4.6$, $p<0.001$) and to the OAR grade scores (Spearman rho=0.51, $p<0.001$). The coefficients of the linear model are shown in Table 1. The linear model of the responsiveness of the qMRI composite index reduced the longitudinal variability of the index in 12%. ($r^2=0.116$, $p<0.001$). The index had an average annualized SRM of 0.14 for the 179 subjects.

<table>
<thead>
<tr>
<th>Coefficients:</th>
<th>Value</th>
<th>Std.Error</th>
<th>t-value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time</td>
<td>0.5054</td>
<td>0.0819</td>
<td>6.1755</td>
<td>0.000000000</td>
</tr>
<tr>
<td>BLoqMRIIndex x Time</td>
<td>-0.121</td>
<td>0.0219</td>
<td>-5.518</td>
<td>0.000000000</td>
</tr>
</tbody>
</table>

**Conclusions:** The image-analysis methodology and biomarker discovery approach presented in this work was able to automatically segment the OAI DESS images and used to provide an objective index of the OA stage that is associated to the WOMAC scores and to the OA grade scores. Furthermore, this index has the potential to be used for automated objective screening for OA progressors. The methodology has still to be validated using more time points. It effectiveness and usefulness has still to be tested in independent OA study cohorts.

**120 MITOCHONDRIAL DNA HAPLOGROUPS MODULATE THE SERUM LEVELS OF BIOMARKERS IN PATIENTS WITH OSTEARTHRITIS**

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**Purpose:** To analyze the influence of mitochondrial DNA (mtDNA) haplogroups on serum levels of molecular biomarkers in patients with osteoarthritis (OA).

**Methods:** We analyzed serum levels of molecular biomarkers of cartilage metabolism (collagen type II markers: ColII-1, ColII-1NO2, C2C, CPII), synovial metabolism (hyaluronic acid (HA)) and cartilage and synovial turnover (YKL-40) in 73 OA cases and 77 healthy controls using enzyme-linked immunosorbsent assays (ELISAs). All subjects had been previously genotyped for the mtDNA haplogroups J, U, and H. Non-parametric and multivariate analysis were performed to test the effects of the clinical variables, including gender, age, smoking status, diagnosis, mtDNA haplogroups and radiologic Kellgren/Lawrence (K&L) grade on the serum levels of the molecular markers.

**Results:** Non parametric analysis showed increased serum levels of HA in patients with OA, meanwhile the values for ColII-1, C2C and C2C/CPII ratio appeared statistically increased in healthy controls. Multivariate analysis showed a clear incidence of the mtDNA haplogroups in the serum levels of the typical type II collagen markers. Carriers of the mtDNA haplogroup H had higher levels and carriers of the mtDNA haplogroup J showed lower levels. Statistical interactions between mtDNA haplogroups and both diagnosis and radiologic K&L grade in the serum levels of the molecular markers were also detected.

**Conclusions:** A new role for mtDNA haplogroups emerges from this work. Our results suggest that the mtDNA haplogroups significantly interact with the serum levels of OA-related molecular markers, suggesting the possibility of their use as a complementary assay with these molecular markers.

**121 SKIN AND URINE PENTOSIDINE AS MARKERS OF RADIOGRAPHIC JOINT DAMAGE IN EARLY OSTEARTHRITIS**

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**Purpose:** Age-related changes in articular cartilage are likely to play a role in the aetiology of osteoarthritis (OA). One of the major age-related changes in cartilage is the accumulation of advanced glycation endproducts (AGEs). Pentosidine is considered to be an adequate marker for the many AGEs formed in vivo. The best way to study the effect of pentosidine on the development of OA is by taking cartilage biopsies. However, this may interfere with the disease process. Therefore, other sources need to be found to overcome this problem. Skin and urine pentosidine may be used as surrogate marker for cartilage pentosidine. The present study describes the presence of AGE in skin and urine in relation to OA severity, in a cohort of patients with very early signs of knee and/or hip OA (CHECK).

**Methods:** Paired skin and cartilage samples were obtained post-mortem (n=17). Furthermore, paired skin and urine samples were obtained from a cohort of 300 patients with knee and/or hip pain being part of the Dutch CHECK cohort. Since urine pentosidine levels can vary in time due to diet variation, urine was collected at 2 different time points with 3 month time interval. Levels of pentosidine as AGE marker were measured in digested skin samples and urine by HPLC. X-rays of both knees (weight bearing, semi flexed) and hips (weight bearing, AP) were made of all patients and scored according to Kellgren and Lawrence (K&L).

**Results:** Cartilage pentosidine correlates well with skin pentosidine (R=0.473, $p<0.001$). Of 205 patients all data could be collected. The number of patients with a K&L grade 0 to 6 of the sum of the 4 joints was 67, 57, 34, 15, 21, 3, 4, 2, and 2. Skin pentosidine was higher in mild (total KL $\leq 4$) compared to low (total KL $< 3$) radiographic OA (p<0.05). A marginal but statistically significant correlation of skin pentosidine levels with the sum K&L score was found. Separating hips and knees, the pentosidine relation with severity of radiographic OA was found for the knee but not for the hip. Skin and urine pentosidine levels correlate marginal (R=0.285, $p<0.05$). For urine pentosidine, no difference could be found between mild and low radiographic OA, even not when separating hips and knees. Age, creatinine clearance, gen-