



Title	Effect of periacetabular osteotomy on the distribution pattern of subchondral bone mineral density in patients with hip dysplasia
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1 **Effect of periacetabular osteotomy on the distribution pattern of subchondral bone mineral**  
2 **density in patients with hip dysplasia**

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15

16 **Running title:** Effect of periacetabular osteotomy

17

18 **Author contributions statement:**

19 Tomohiro Shimizu contributed to research design, data acquisition, analysis and interpretation of  
20 data, and drafting of the paper; Daisuke Takahashi contributed to data acquisition and analysis  
21 and interpretation of data; Yumejiro Nakamura contributed to data acquisition and analysis and  
22 interpretation of data; Takuji Miyazaki contributed to data acquisition; Shunichi Yokota  
23 contributed to data acquisition; Hotaka Ishizu contributed to data acquisition; Norimasa Iwasaki

24 contributed to interpretation of data. All authors have read and approved the final submitted  
25 manuscript.

26

27

28 **Abstract**

29 Despite the availability of long-term follow-up data, the effect of pelvic osteotomy on the natural  
30 history of osteoarthritis is not yet fully understood, partly because there is untapped potential for  
31 radiographs to better describe osteoarthritis. Therefore, this study aimed to assess the distribution  
32 of subchondral bone mineral density (BMD) across the acetabulum in patients with hip dysplasia  
33 immediately (2 weeks) and 1 year after undergoing periacetabular osteotomy (PAO). To that end,  
34 we reviewed 40 hips from 33 patients with developmental dysplasia of the hip (DDH) who  
35 underwent PAO between January 2016 and July 2019 at our institution. We measured  
36 subchondral BMD through the articular surface of the acetabulum using computed tomography  
37 (CT) osteoabsorptiometry (OAM), dividing the distribution map into nine segments. We then  
38 compared the subchondral BMD between 2 weeks and 1 year after PAO in each area. At 2 weeks  
39 after PAO, the high-density area tended to be localized particularly in the lateral part of the  
40 acetabulum, whereas 1 year after PAO, the high-density area moved to the central and lateral  
41 parts. The percentage ratios of the subchondral BMD for the central-posterior, lateral-central, and  
42 lateral-posterior areas relative to the central-central area were significantly decreased at 1 year  
43 after PAO, as compared to those at 2 weeks after PAO. These findings suggest that loading was  
44 altered by PAO to be more similar to physiological loading. Long follow-up observational study  
45 is warranted to confirm the association between early changes in subchondral BMD by PAO and  
46 joint degeneration.

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49

50 **Keywords:** hip dysplasia, bone mineral density, periacetabular osteotomy

51 **Introduction**

52 Developmental dysplasia of the hip (DDH) with associated structural instability is one of the  
53 more common causes of secondary osteoarthritis<sup>1,2</sup>. Deficiency of the bony acetabulum results in  
54 hip instability and acetabular rim overload with subsequent damage to the labrum and articular  
55 cartilage<sup>3</sup>. Finite element analysis (FEA) has shown that DDH models showed stress  
56 concentration in the acetabular edge and contacting femoral head, as compared to the normal hip  
57 joint model<sup>4</sup>. As such, reducing articular cartilage contact stress by pelvic osteotomy may delay  
58 the appearance or reduce the severity of osteoarthritis<sup>5,6</sup>. Multiple types of pelvic osteotomies  
59 have been described, with intermediate- and long-term clinical and radiographic results,  
60 suggesting that these procedures can prevent the progression of DDH to secondary  
61 osteoarthritis<sup>7-10</sup>. However, despite the availability of long-term follow-up data, the effect of  
62 pelvic osteotomy on the natural history of osteoarthritis is not yet fully understood, partly  
63 because there is untapped potential for radiographs to better describe osteoarthritis.

64         The pattern of subchondral bone density reportedly reflects the distribution of cumulative  
65 stresses acting on a joint surface under actual loading conditions<sup>11</sup>. As early changes in the  
66 subchondral bone can predict subsequent symptoms or disease structural progression, new tools  
67 may help clinicians to stratify different osteoarthritis phenotypes based on bone remodeling  
68 status<sup>12</sup>. Given this theoretical background, Müller-Gerbl et al. have developed a method of  
69 computed tomography (CT) osteoabsorptiometry (CTOAM) to assess the long-term stress  
70 distribution of individual joints in living subjects by measuring subchondral bone density as a  
71 surrogate for cumulative stress and loading abnormalities<sup>11, 13</sup>. Using this method, previous  
72 studies have evaluated the stress distribution of different joints under various loading conditions,  
73 from normal to pathologic or postoperative conditions<sup>14-18</sup>. Focusing on the hip joint, a previous

74 study reported significant differences in the severity and patterns of loading based on the severity  
75 of dysplasia, as compared to the control group<sup>18</sup>. Therefore, CTOAM could detect the effect of  
76 pelvic osteotomy, as the subchondral bone mineral density (BMD) changes over time after PAO  
77 would be a good surrogate measure for loading changes.

78 We hypothesized that periacetabular osteotomy (PAO) would change the distribution of  
79 subchondral bone density across the acetabulum. In the present study, a modified method of  
80 CTOAM was employed to test this hypothesis<sup>19, 20</sup>. Thus, this study aimed to assess the  
81 distribution of subchondral BMD across the acetabulum in patients with DDH immediately (2  
82 weeks) and 1 year after undergoing PAO.

83

## 84 **Methods**

### 85 *Subjects*

86 This study was retrospective cohort study (level of evidence, level III). This study was  
87 conducted in accordance with the ethical standards of the Declaration of Helsinki and was  
88 approved by our Institutional Review Board (#017-0508). A total of 41 hips from 34 patients (4  
89 males and 30 females) with DDH underwent PAO between January 2016 and July 2019 at our  
90 institution. This study only included 40 hips, excluding one patient who delayed rehabilitation  
91 due to fracture of the posterior column. The mean age of the patients at surgery was 32.8 years  
92 (range, 14–55 years), and the mean body mass index (BMI) was 23.1 kg/m<sup>2</sup> (range, 17.8–37.9  
93 kg/m<sup>2</sup>) (Table 1). Surgical indications for PAO included acetabular dysplasia with a lateral center  
94 of edge (CE) angle <20° and discontinuity of the Shenton's line<sup>21</sup>, unsuccessful 6-month  
95 nonoperative treatment, age <60 years, an excellent or grade of the preoperative joint congruency  
96 in abduction according to classification of joint congruency described by Yasunaga<sup>22</sup>, and no

97 pain on hip flexion and extension with the extremity held in abduction<sup>23</sup>.

98 ***Surgery and rehabilitation***

99 All osteotomies were performed by one of four board-certified, fellowship-trained  
100 orthopedic surgeons at a single institution. The type of PAO used was eccentric rotational  
101 acetabular osteotomy (ERAO)<sup>23</sup>, an improved version of rotational acetabular osteotomy<sup>24</sup>. The  
102 operative techniques have been described previously<sup>23</sup>. Briefly, a 20-cm curved skin incision was  
103 made 5 cm proximal to the tip of the greater trochanter. The greater trochanter was then retracted  
104 proximally after completion of osteotomy at its base, with an approximate thickness of 10–15  
105 mm, and the gluteus minimus and medius muscles were reflected approximately 30 mm from the  
106 acetabular rim. The osteotomy site was approximately 15–20 mm or greater from the joint space  
107 according to the preoperative planning. Following osteotomy of the ilium and pubis, the  
108 acetabular fragment was rotated easily, wherein trimming of the inner cortex of the ilium was  
109 essential for medializing the acetabular fragment. Coverage of the femoral head by the rotated  
110 acetabular fragment was verified using an image intensifier before fixation of the acetabular  
111 fragment with two or three polylactide screws. Afterwards, the greater trochanter was  
112 repositioned and fixed with two AO cancellous screws. Postoperatively, one-third partial weight-  
113 bearing was permitted with a walker after 4 weeks, one-half partial weight bearing was permitted  
114 after 6 weeks, and full weight-bearing was allowed after 8 weeks. One year after PAO, the  
115 patients underwent surgery to remove the two AO cancellous screws.

116 ***Clinical and radiological evaluation***

117 Clinical evaluations were performed using the Harris hip score (HHS)<sup>25</sup> and the Japanese  
118 Orthopedic Association Hip-Disease Evaluation Questionnaire (JHEQ)<sup>26</sup> preoperatively and 1  
119 year after PAO. Range of motion was measured by goniometry. Supine anterior–posterior (AP)

120 pelvic radiographs and CT scans were taken preoperatively, 2 weeks after PAO, and 1 year after  
121 PAO (average radiation exposure per examination, 5.5 mSv). The radiographs were obtained  
122 using Siebenrock's standardized technique<sup>27</sup>, and the CE angle, Sharp angle, acetabular head  
123 index (AHI)<sup>28</sup>, and acetabular roof obliquity (ARO) were evaluated<sup>29</sup>. All digital measurements  
124 and calculations were performed using the Centricity™ Web-J 3.0 HD software (GE Healthcare  
125 Japan, Tokyo, Japan). Measurements were performed two times with a 3-month interval by the  
126 first two authors (T.S. and N.Y.), showing almost excellent intra- and inter-class correlation  
127 coefficients (0.943,  $P < 0.001$ , and 0.873,  $P < 0.001$ ; respectively). A high-resolution (pixel  
128 matrix,  $512 \times 512$ ) helical CT scanner (CT High Speed Advantage; GE Medical Systems,  
129 Milwaukee, WI, USA) was used to obtain axial images of the bilateral hips with an intensity  
130 calibration phantom (B-MAS200, Kyoto Kagaku, Kyoto, Japan). The slice thickness and interval  
131 were set to 1 mm each, and the table speed was set to 1 mm/s. Imaging data were analyzed using  
132 the Aquilion One image analysis system (Toshiba Medical Systems, Tokyo, Japan), and a three-  
133 dimensional bone model was generated from the axial image stack. Thereafter, anterior pelvic  
134 plane-based coronal views at 1-mm intervals were reconstructed using the multiplanar  
135 reconstruction model.

136 To evaluate subchondral bone density, we used OsteoDens 4.0, a noncommercial  
137 software developed at our institution<sup>16-19</sup>. The target area was the subchondral bone region of the  
138 weight-bearing acetabular surface. In the coronal image, the region-of-interest was manually  
139 selected to include the entire subchondral bone layer of the acetabulum in all slices, numbering  
140 an average of 102.4 coronal slices (range, 92–115 slices) to capture the acetabulum. After  
141 establishing the region-of-interest, we automatically measured the subchondral bone of the  
142 undersurface of the acetabular at each coordinate point at 1-mm intervals in Hounsfield units



143 (HU), which is defined as the radiograph attenuation whereby water is 0 and compact bone is  
144 1000 (Fig. 1). Measurement and mapping were repeated in each slice, and the data were stacked  
145 to create a two-dimensional mapping image showing the distribution of subchondral bone  
146 density. We then divided the acetabulum automatically into three equal parts following the front-  
147 back and medial-lateral directions, and the measured target area was divided into nine regions:  
148 medial anterior (MA), medial central (MC), medial posterior (MP), central anterior (CA), central  
149 center (CC), central posterior (CP), lateral anterior (LA), lateral central (LC), and lateral  
150 posterior (LP) (Fig. 1B). The mean bone density, corrected using the phantom (B-MAS200,  
151 Kyoto Kagaku, Kyoto, Japan), was measured for each region. Additionally, to evaluate the  
152 distribution, we investigated the ratios of the subchondral BMD of each area to that of the CC  
153 area.

154 Furthermore, we calculated the intra- and interobserver reproducibility of the CTOAM  
155 based on the five consecutive measurements and based on the measurements of the two  
156 orthopedic surgeons (T.S. and N.Y.), respectively. The reliabilities between and within each  
157 observer were calculated according to the intraobserver, interobserver, and residual variances  
158 estimated by the analysis of variance table based on Proc Mixed in the SAS software (SAS  
159 Institute, Cary, NC, USA). The intra-class correlation coefficients for intra- and interobserver  
160 reproducibility were 0.86 (95% confidence interval [CI], 0.73–0.97) and 0.79 (95% CI, 0.65–  
161 0.91), respectively.

### 162 ***Statistical analysis***

163 Paired *t*-tests with Bonferroni correction were used to compare the clinical evaluation and  
164 BMD of the subchondral bone preoperatively, 2 weeks after PAO, and 1 year after PAO.  
165 Correlations between BMI and subchondral BMD were performed using Pearson's product–

166 moment correlation coefficient. All statistical analyses were performed using the IBM SPSS  
167 version software (SPSS Inc., Chicago, IL, USA), and statistical significance was set at  $p < 0.05$ .

168

## 169 **Results**

### 170 *Demographic characteristics, clinical score, and radiographic parameters*

171 Table 1 summarizes the longitudinal clinical scores and radiographic parameters in this  
172 study. Although internal rotation was limited at 1 year postoperatively ( $P = 0.005$ ), clinical  
173 scores, including the HHS and JHEQ, were significantly improved, as compared to those  
174 preoperatively ( $P < 0.001$ ). The mean CE angle and mean AHI increased, whereas the mean  
175 Sharp angle and mean ARO decreased significantly from the preoperative to postoperative values  
176 (all  $P < 0.001$ ).

### 177 *Analysis of patients treated with PAO*

178 At 2 weeks after PAO (immediately after surgery), the high-density area tended to be  
179 localized in the lateral part of the acetabulum (Fig. 2A), whereas at 1 year after PAO, the high-  
180 density area moved to the central and lateral parts. In the quantitative evaluation of the  
181 subchondral BMD calibrated according to the phantom, mean BMD values in the medial, CA,  
182 and CC areas at 1 year after PAO were significantly higher than those at 2 weeks after PAO (Fig.  
183 2B). To evaluate subchondral BMD distribution, we investigated the ratios of the subchondral  
184 BMD of each area to that of the CC area (Fig. 2C). The percentage ratios of the subchondral  
185 BMD for the CP, LC, and LP areas relative to the CC area were significantly decreased at 1 year  
186 after PAO, as compared to those at 2 weeks after PAO. No significant associations between BMI  
187 and subchondral BMD were observed (Supplemental Table 1).

188

189 **Discussion**

190 Clinically, PAO has been reported to be an effective treatment for early osteoarthritis in young or  
191 active patients with DDH<sup>30-32</sup>. Moreover, this study showed the significant improvement of HHS  
192 and patient-based clinical outcomes (JHEQ) from preoperative to 1 year after surgery. Despite  
193 this, although simulation studies using finite or discrete element analysis showed alterations of  
194 contact stress by PAO<sup>4,33</sup>, findings on changes in the mechanical environment due to PAO have  
195 not yet been fully clarified. In this study using CTOAM, we found that PAO shifted the area with  
196 the highest subchondral BMD from the lateral to the central region and reduced the ratio of  
197 subchondral BMD in the CP, LC, and LP areas relative to that in the CC area, thus confirming  
198 our hypothesis.

199 The finding that the subchondral BMD on the lateral side tended to be higher than that on  
200 the medial and center areas at 2 weeks after PAO showed a similar tendency to a previously  
201 described study on severe dysplasia subjects<sup>18</sup>, suggesting that CTOAM data at 2 weeks after  
202 PAO may reflect the preoperative mechanical environment. Moreover, the finding that the  
203 subchondral BMD in the central area tended to be higher than that in other areas at 1 year after  
204 PAO showed a similar tendency to the control subjects ( $25^\circ < \text{CE angle} < 35^\circ$ ) of that same  
205 study<sup>18</sup>. Although one of the main limitations of the current study was the indirect measure of  
206 mechanical stress with acetabular subchondral BMD using CTOAM, we believe that these  
207 findings suggest that loading was altered by PAO to be more similar to physiological loading.

208 Contrary to our expectations and previous reports using FEA<sup>34,35</sup>, this study showed that  
209 the absolute subchondral BMD in the medial, CA, and CC areas increased significantly from 2  
210 weeks to 1 year after PAO. Since PAO transfers the medial part, which is considered to be a  
211 lower mechanical stress area, to the central area, it is possible that the subchondral BMD in the

212 medial and central areas were relatively low at 2 weeks after PAO. Furthermore, it is possible  
213 that this finding may have been affected by the limitation of weight-bearing immediately after  
214 PAO. However, since this study was only a 1-year longitudinal follow-up study, a longer follow-  
215 up period is necessary to address whether the increase in subchondral BMD from 2 weeks to 1  
216 year after PAO would affect future joint degeneration.

217         Despite these findings, this study had a few limitations. First, we could not directly  
218 measure the contact stress pressure and stress distribution patterns in the live patients' hips.  
219 However, the measurements of BMD were more clinically accessible. Second, although we  
220 performed fixation of the acetabular fragment with two or three polylactide screws and compared  
221 the CT data on the same setting between 2 weeks and 1 year after PAO, the artifact from the  
222 screws could have affected BMD distribution in this setting. Third, postoperative alterations in  
223 the pattern of subchondral bone mineralization may depend not only on the biomechanical  
224 effects of PAO but also on the individual loading conditions. To clarify this point, we should  
225 perform further analysis based on CT data from more patients treated with PAO. Fourth, this was  
226 a short follow-up observational study. Although we targeted the early changes in the subchondral  
227 bone during PAO, a longer follow-up study is required to understand the association between  
228 subchondral BMD and joint degeneration. Finally, because reductions in vascular supply are  
229 associated with bone loss<sup>36</sup>, BMD may also depend on the vascularity of the acetabular fragment.  
230 As this study did not investigate the vascularity of the acetabular fragment, further studies should  
231 address this concern in the future.

232         In conclusion, the findings of this study using the CTOAM method suggest that loading  
233 was altered by PAO to be more similar to physiological loading. Long follow-up observational

234 studies should be performed to confirm the association between early changes in subchondral  
235 BMD by PAO and joint degeneration.

236

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240 Conflicts of Interest: The authors declare that they have no conflict of interest.

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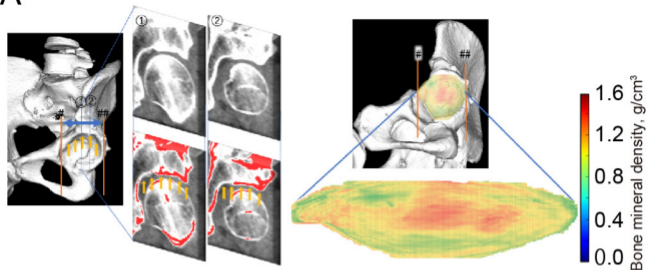
341 **Figure legends**

342 **Fig. 1.** (A) The image shows how the subchondral bone region of the acetabulum was identified  
343 automatically using the customized software. In each coronal slice, we measured the Hounsfield  
344 units of radiograph absorption in the subchondral bone at each coordinate point in 1-mm  
345 intervals. For quantitative analysis, the distribution pattern is represented as a surface-mapping  
346 image depicted by a color scale. (B) The image shows segments used for quantitative analysis of  
347 the bone density mapping data for the acetabulum.

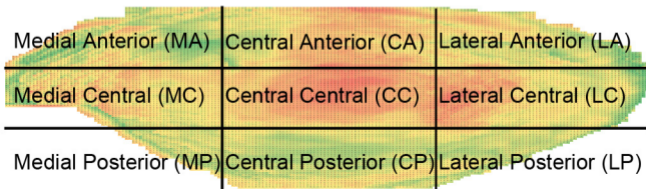
348 **Fig. 2.** (A) The images show the distribution of bone density values across the articular surface  
349 of the acetabulum at 2 weeks and 1 year after periacetabular osteotomy. (B) Comparisons of the  
350 subchondral bone mineral density between 2 weeks and 1 year after periacetabular osteotomy in  
351 each area. (C) Comparisons of the percentage ratio of each area relative to the subchondral bone  
352 mineral density in the central center area between 2 weeks and 1 year after periacetabular  
353 osteotomy. Data are presented as means  $\pm$  standard deviation. Asterisks indicate  $P < 0.05$ .

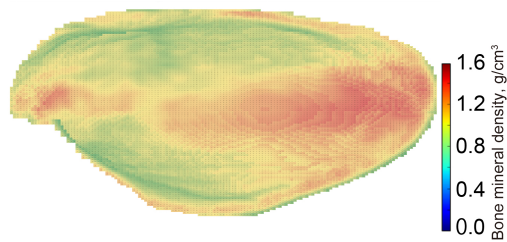
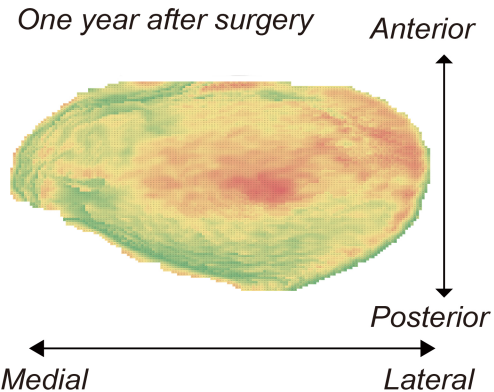
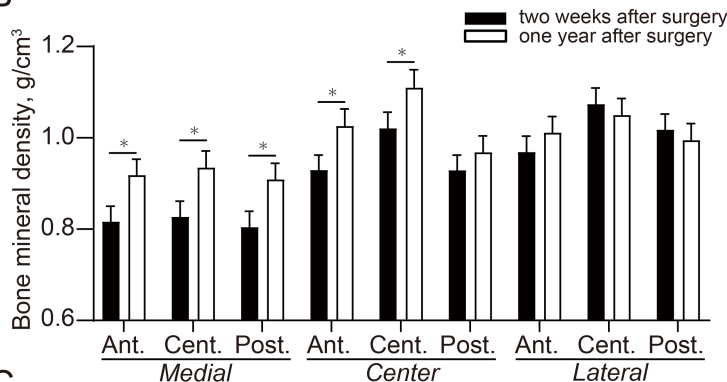
354  
355  
356  
357  
358

A



B



**A***Two weeks after surgery**One year after surgery***B****C**