

Observational Study



Subchondral Bone Changes Following Sacroiliac Joint Arthrodesis – A Morpho-mechanical Assessment of Surgical Treatment of the Painful Joint

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Background: Sacroiliac joint arthrodesis is an ultima ratio treatment option for sacroiliac joint dysfunction. Fusion drastically reduces sacroiliac joint movement providing long-lasting pain-relief associated with tension-relief to the innervated sacroiliac joint structures involved in force closure.

Objectives: To display the bone mineralization distribution patterns of the subchondral bone plate in 3 distinct regions (superior, anterior, and inferior) of the sacral and iliac counterparts of the sacroiliac joint pre- and post-sacroiliac joint arthrodesis and compare patterns of sacroiliac joint dysfunction post-sacroiliac joint fusion with sacroiliac joint dysfunction pre- arthrodesis patterns and those from healthy controls.

Study Design: An observational study.

Setting: The research took place at the University of Basel, Switzerland, where the specific image analysis program (Analyze, v7.4, Biomedical Imaging Resources, Mayo Foundation, Rochester, NY, USA) was made available.

Methods: Mineralization densitograms of 18 sacroiliac joint dysfunction patients pre- and post-sacroiliac joint arthrodesis (≥ 6 , ≥ 12 , and ≥ 24 months post-surgery) were obtained using computed tomography osteoabsorptiometry. For each patient, pre- vs. post-surgery statistical comparisons were undertaken, using the Hounsfield unit values derived from the subchondral mineralization of superior, anterior, and inferior regions on the iliac and sacral auricular surfaces. Post-operative values were also compared to those from a healthy control cohort ($n = 39$).

Results: In the pre-operative cohort at all 3 follow-up times, the superior iliac region showed significantly higher Hounsfield unit values than the corresponding sacral region ($P < 0.01$). Mineralization comparisons were similar for the sacrum and ilium in the anterior and inferior regions at all follow-up points ($P > 0.5$) with no surgery-related changes. Sacral density increased significantly in the post-operative state; not observed on the ilium. Post-operative sacroiliac joints showed a significantly increased mineralization in the superior sacrum after ≥ 6 months ($P < 0.05$), not replicated after ≥ 12 nor ≥ 24 months. Further comparison of post-operative scans versus healthy controls revealed significantly increased mineralization in the superior sacral region at (≥ 6 , 12, and 24 months ($P < 0.01$), likely related to bone grafting, and in the anterior and inferior regions in post-operative scans at ≥ 12 and ≥ 24 months follow-up ($P < 0.05$).

Limitations: The given study is limited in sample size. Post-operative computed tomography scans had screws which may have left artifacts or partial volume effects on the surfaces. Healthy controls were different patients to the sacroiliac joint dysfunction and post-operative cohorts. Both cohorts were age-matched but this comparison did not take into account potential population differences. Size differences in the regions may have also been an influencing factor of the results as the regions were based on the size and shape of the articular surface.

Conclusions: Sacroiliac joint arthrodesis results in an increased morpho-mechanical conformity in the anterior and inferior sacrum and reflects variable morpho-mechanical density patterns compared to the healthy state due to permanent alterations in the kinematics of the posterior pelvis.

Key words: Bone mineral density, bone mineralization, computed tomography, Hounsfield units, osteoabsorptiometry, sacroiliac, sacroiliac joint arthrodesis, sacroiliac joint fusion, sacroiliac joint dysfunction, subchondral bone plate

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Sacroiliac joint dysfunction (SIJD) affects 13%—32% of the patients suffering from chronic lower back pain (1,2). Biomechanical disorders such as hypo- or hypermobility, misalignment, or subluxation (3,4) of the sacroiliac joint (SIJ) could cause lower back and buttock pain. SIJ arthrodesis is one treatment option for severe and persistent cases of chronic SIJ pain after substantial conservative therapies fail (5). Either open and minimally invasive techniques of SIJ arthrodesis provide longer lasting pain-relief allowing patients to resume a more active life-style such as the return to work or sports (2,6-8). Although surgical treatments may involve several complications such as nerve injury or a surgical site infections, it is often the last resort for patients with chronic SIJ pain.

There is preliminary evidence that surgical SIJ fusion drastically reduces movement at the joint by > 50% in all 3 anatomical planes (9). Reduction of joint movement lowers the stress of innervated SIJ-related ligaments, muscles, and bones that would contribute to SIJ pain-relief (10,11). On the other hand, SIJ arthrodesis could also alter stresses and loads on the auricular surfaces of the SIJ and the underlying subchondral bone plate, affecting the mineralization patterns due to the alteration of SIJ biomechanics.

The subchondral bone plate of the SIJ helps transmit forces passing through the joint to the underlying cancellous bone (12,13), thereby dissipating resulting stresses to broader areas. Gradual increase of subchondral bone mineralization to adapt to repeated mechanical loading can be evaluated in computed tomography (CT) osteoabsorptiometry (OAM) (14-17). Based on conventional CT scans, this method provides color-mapped densitograms using Hounsfield units (HU) to illustrate the bone mineralization of a surface (9,12,18-24) and reflects the biomechanical properties of the subchondral bone, as shown by our group in an elderly cohort (17).

This study aimed to display the bone mineralization distribution patterns of the subchondral bone plate in 3 distinct regions (superior, anterior, and inferior) of the sacral and iliac counterparts of the SIJ pre- and post-SIJ arthrodesis. This will allow for the quantification analysis of altered density patterns that relate to SIJ arthrodesis to then compare these patterns with those from the scans pre-SIJ fusion. Furthermore, a comparison with healthy joints will be undertaken to determine if surgery alters mineralization back to the patterns observed in a healthy state.

The following hypotheses were investigated:

1. Following SIJ arthrodesis, there is a trend towards conformity of bone mineralization patterns across the 3 regions of the subchondral bone plate of the joint.
2. Bone density increases as a consequence of SIJ arthrodesis throughout the SIJ compared to the pre-operative dysfunctional state due to the joint fusion.
3. Bone adaptations related to SIJ arthrodesis reflect different distribution patterns than healthy joints.

METHODS

Patients with SIJD

SIJ arthrodeses were performed in 18 patients diagnosed with uni- or bilateral SIJD (9 women; 9 men; range 45 ± 14 years) at JCHO Sendai Hospital, Sendai, Japan (Fig. 1).

Definitive diagnosis of SIJD was confirmed by > 70% pain relief at the SIJ region after local anesthetic injections to the SIJ (25). Patients with histories of infection, lumbopelvic tumors, lumbar spine and pelvic fractures, and seronegative spondylarthropathy were excluded. All patients had a history of previous injections including selective nerve root infiltration and/or lumbar disc nerve block that were negative. All patients reached the standard of indication for SIJ arthrodesis as ultima ratio treatment: insufficient responsiveness to conservative treatments continued for > 6 months, difficulties in physical activities, and/or marked restrictions of daily living due to recurrence of severe SIJ pain, even after undergoing repeated diagnostic/therapeutic injections and substantial physical therapy (5). SIJ arthrodesis was performed either unilaterally or bilaterally, corresponding to the side of dysfunction. Five patients were operated on using an anterior approach (Fig. 2A), 8 a posterior approach (Fig. 2B), and 3 a combination of anterior and posterior approaches, one had pelvic ring fusion (additional fusion of the pubic symphysis) and one underwent lateral fusion. One patient with bilateral SIJD underwent unilateral fusion, therefore the contralateral un-fused but painful side was excluded from the analysis. Follow-up CT scans were done ≤ 6 months to ≥ 4 years after the surgery. Study size was based on all patients enrolled between the recruitment period (Cohen's d = 0.22).

In addition, a control cohort of 39 age-matched CT scans (20 women, 19 men: range 55 ± 18 years) was used to represent a healthy control used in a previous study

(17). None of these cases had a current or past history of lower back pain, SIJ-related pathology, nor abnormalities on their medical records. The Institute Review Board of JCHO Sendai Hospital, Sendai, Miyagi, Japan (no. 2019-1) approved the present study. All experiments were conducted according to the Declaration of Helsinki.

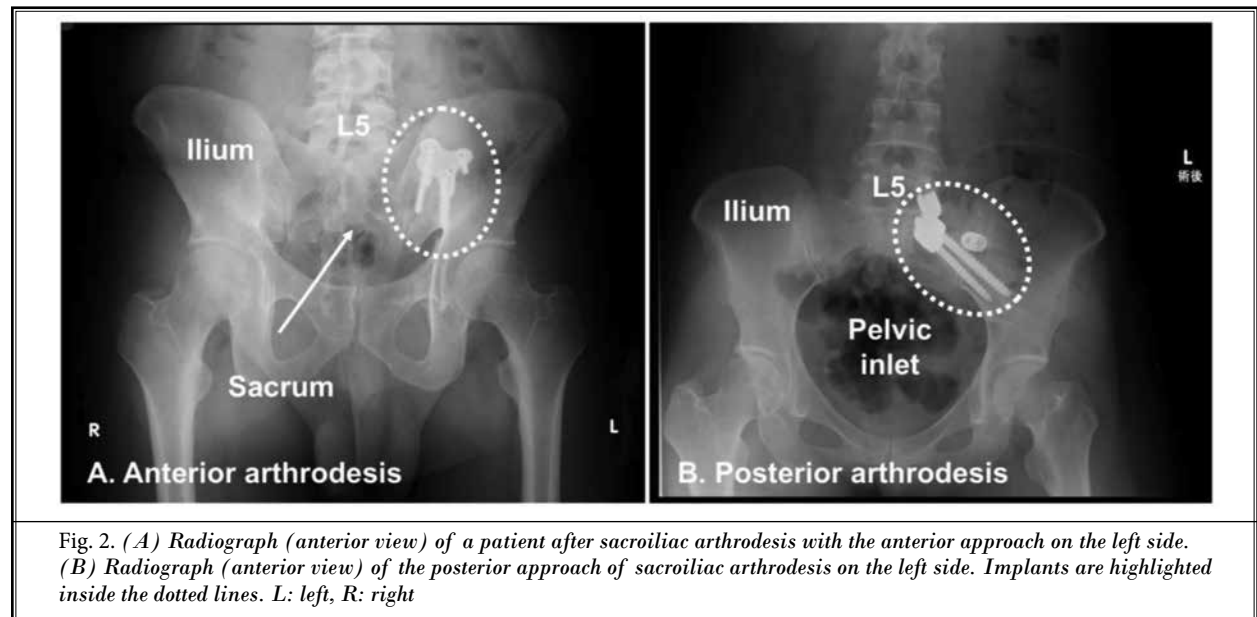
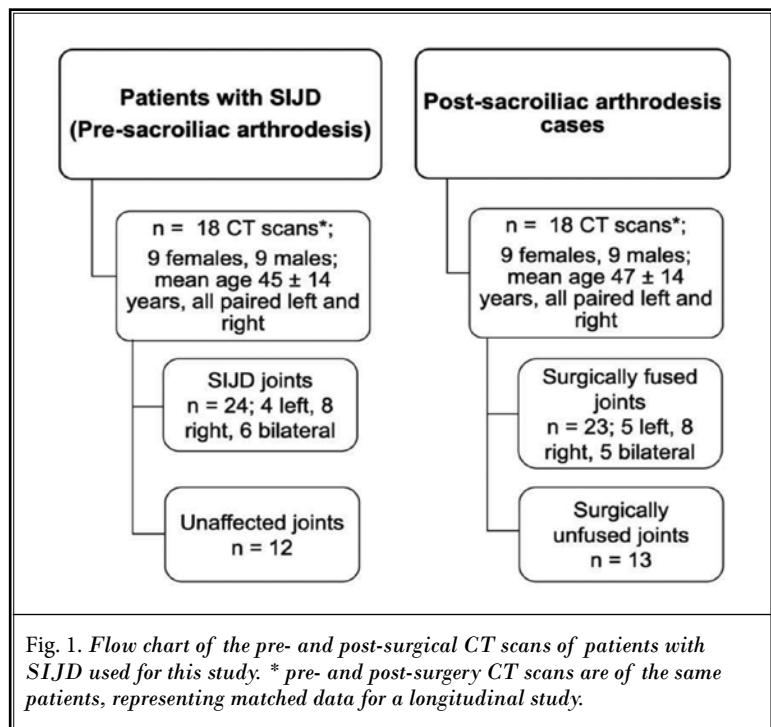
Computed Tomography Osteoabsorptiometry of the SIJ

Data sets for CT-OAM were derived from conventional CT (Aquilion one, Toshiba, Tokyo, Japan). Slices thickness ranged from 0.7 to 5.0 mm depending on the scan. CT-OAM was evaluated using a specific image analysis program (Analyze, v7.4, Biomedical Imaging Resources, Mayo Foundation, Rochester, NY, USA). The sacral and iliac sides of each SIJ were manually segmented before the data were false color-coded and superimposed on the 3-dimensionally reconstructed ilia and sacra for anatomical localization of the mineralization as densitograms (17,26). The maximum intensity projection revealed the HU of each pixel (23) and threshold values were chosen according to previous studies to be ≤ 200 to ≥ 1200 HU (12,17,26). Screws, plates, and other surgical elements observed on the post-operative scans were

manually segmented out to remove potential bias introduced by artifacts on the scans. This resulted in visible holes in the final densitograms.

Analysis of Densitogram Patterns of the SIJ

The mineralization patterns of the iliac and sacral



sides were evaluated based on the mean HU values of the regions on the densitogram for each dataset. The auricular surfaces were subdivided into 3 regions: the superior, anterior, and inferior (Fig. 2). These were established anatomically by one author (AP) by isolating the anterior region which included the apex of joint, the other 2 regions were created based on this. The size of the region segmenting tool was based on the size of the auricular surface of the specimen. Calculation of the mean HU value for each region was computed and these values were subsequently statistically compared between the different groups.

The post-operative cohort comprised of ≥ 6 months follow-up scans post-surgery. From this cohort, follow-up scans of 3 sub-groups were derived for (≥ 6) (n = 24), (≥ 12) (n = 17), and (≥ 24) months (n = 13). For statistical analyses, GraphPad Prism (version 8, San Diego, CA, USA) was used. Statistical significance was defined at the 5% ($P < 0.05$) level. Gaussian distribution was first assessed using a Shapiro-Wilk test. Depending on data distribution, a one-way ANOVA or a Kruskal-Wallis test without Dunn's post-hoc correction was undertaken for the multiple assessment of paired data between the 3 regions. Mean HU values were reported \pm standard deviation, [95% confidence interval (CI): upper bound, lower bound]. For pre- vs. post-surgery comparisons, the corresponding pre-operative scan was compared with the respective post-operative scan of the same patient using a Friedman or paired data- ANOVA test to compare paired-results.

RESULTS

In the post-operative cohort, scans that seemed more affected by unwanted artifacts and holes left after the manual segmentation were initially removed. A statistical analysis was made comparing this reduced cohort (n = 10) with the initial complete cohort (n = 23). No statistically significant difference was found in the results due to the artifacts ($P = 0.2$); therefore, all scans were included in the study.

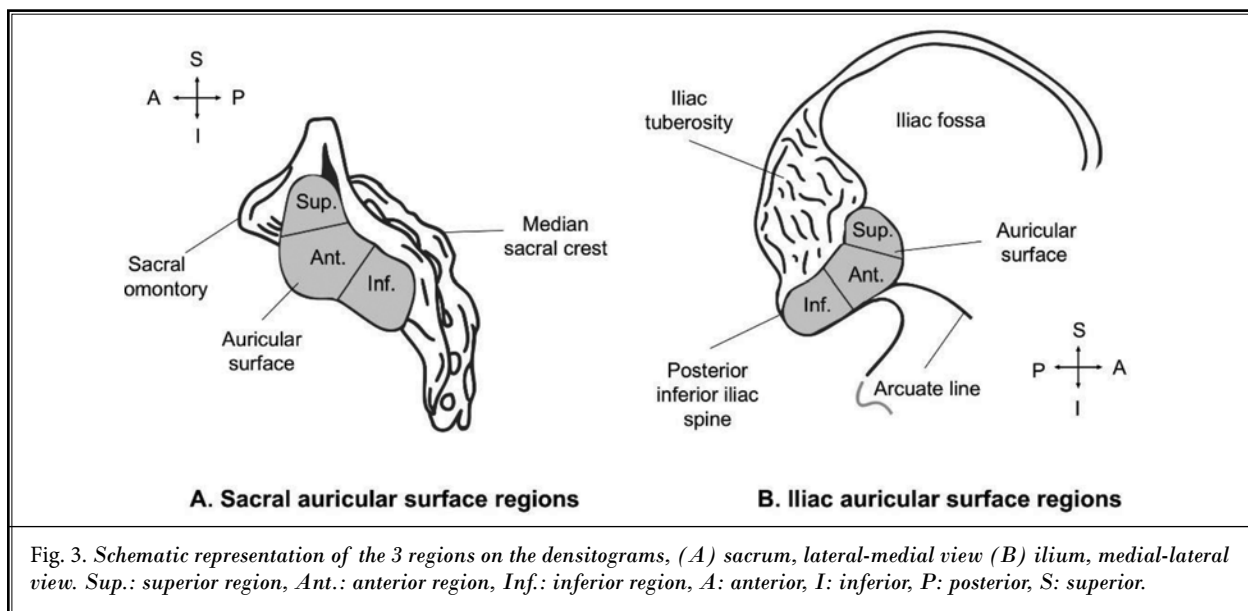
Morphological Density Conformity Exists Between Iliac and Sacral Sides in the Anterior and Inferior Regions

In the pre-operative cohort, the superior region in the ilium showed significantly higher mineralization values than the corresponding region of the sacrum ($P < 0.01$), indicated by the HU values (Fig. 3A).

At all 3 post-operative follow-up scans (≥ 6 , ≥ 12 , and ≥ 24 months), the higher mineralization in the superior region of the ilium side was observed ($P < 0.01$; Fig. 3B). On the other hand, mean HU values were similar in the anterior and inferior regions in comparison with the sacral and the iliac sides at pre- and all follow-up scans (Fig. 3) in the post-operative state.

Sacral Subchondral Bone Mineralization Increased in the Superior and Anterior SIJ Post-surgery

When comparing the mineralization patterns of the pre- and post-operative SIJ, the bone mineral den-



sity of the 3 sacral sub-regions increased in the post-operative state at all follow-up time points. Analysis in the 6 months follow-up sub-group ($n = 23$), mean sacral HU values of the sacrum significantly increased from 581 ± 179 HU [95% CI: 504, 659] pre-operatively to 670 ± 142 HU [95% CI: 608, 731] post-operatively ($P < 0.05$). There were no significant differences in the other regions of the sacrum side; the anterior region was 662 ± 176 HU [95% CI: 586, 738] pre-operatively and 689 ± 165 HU [95% CI: 618, 760] post-operatively ($P = 0.4$) and the inferior region was 516 ± 109 HU [95% CI: 469, 563] pre-operatively and 520 ± 88 HU [95% CI: 482, 558] post-operatively ($P = 0.8$). An example of a representative case is given in Fig. 4A. Furthermore, the post-operative joints showed a temporary significant increasing HU value in the superior sacral region at 6 months post-surgery ($P < 0.05$) which was not replicated at 12 nor 24 months post-operatively ($P = 0.1$).

Regarding the iliac side, HU values did not increase significantly in any sub-region at 6, 12 (Fig. 4B), nor 24 months (Fig. 4B; supplementary Tables 1 and 2): The superior region was 893 ± 214 HU [95% CI: 800, 985] pre-operatively and 851 ± 160 HU [95% CI: 782, 921] post-operatively ($P = 0.9$), the anterior region was 760 ± 165 HU [95% CI: 689, 832] pre-operatively and 756 ± 163 HU [95% CI: 685, 826] post-operatively ($P = 0.9$), and the inferior region was 550 ± 144 HU [95% CI: 488,

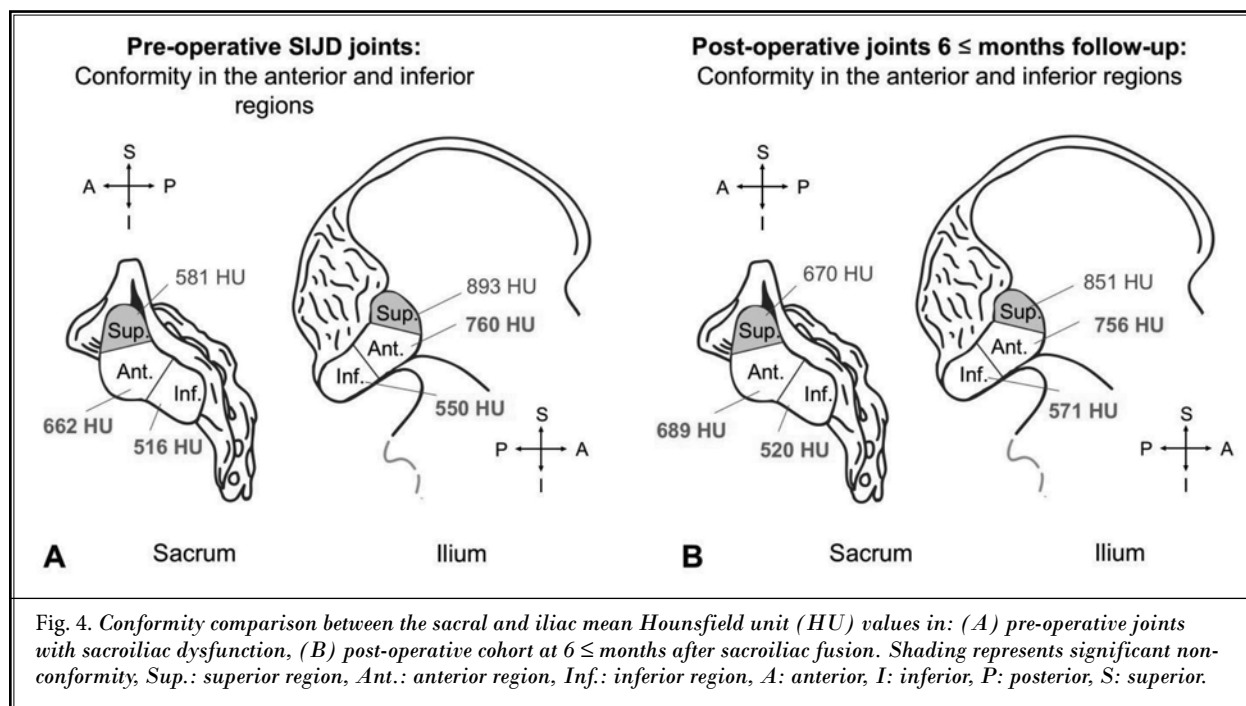
613] pre-operatively and 571 ± 175 HU [95% CI: 496, 647] post-operatively ($P = 0.6$).

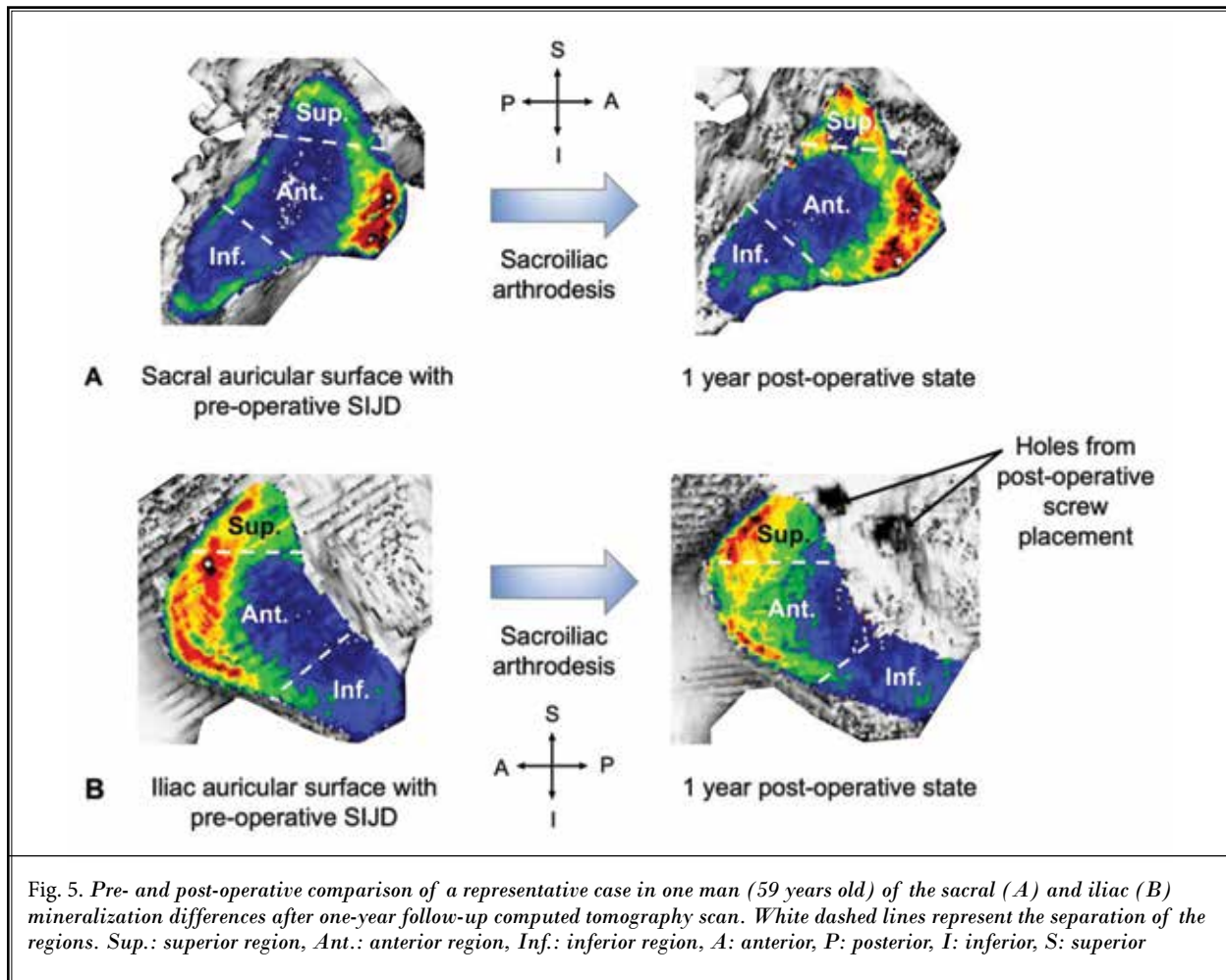
Mineralization Differences Change with Time in the Superior Sacrum Resulting from SIJ Fusion When Compared to Healthy Joints

When comparing the post-operative joints with healthy controls at the 3 time points, HU values were significantly higher in the superior sacrum in the 6 month follow-up subgroup and in the 12 months follow-up subgroup as well (both $P < 0.01$). In the 24 months follow-up subgroup, HU value in all 3 regions in the sacrum side showed significantly higher HU values than the healthy joints ($P < 0.05$; Fig. 5). Comparisons between the HU values of the post-operative cohort at each time frame revealed no significant differences between regions ($P = 0.5$).

DISCUSSION

This study quantified SIJ subchondral bone density using CT-OAM in SIJD patients pre- and post-operatively. These findings are based on a morpho-mechanical link demonstrated for the subchondral bone mineralization patterns and related mechanical properties. The mineralization patterns presented here are likely the result of chronically recurring loading conditions of individuals with SIJD and after SIJ fusion, presenting marked



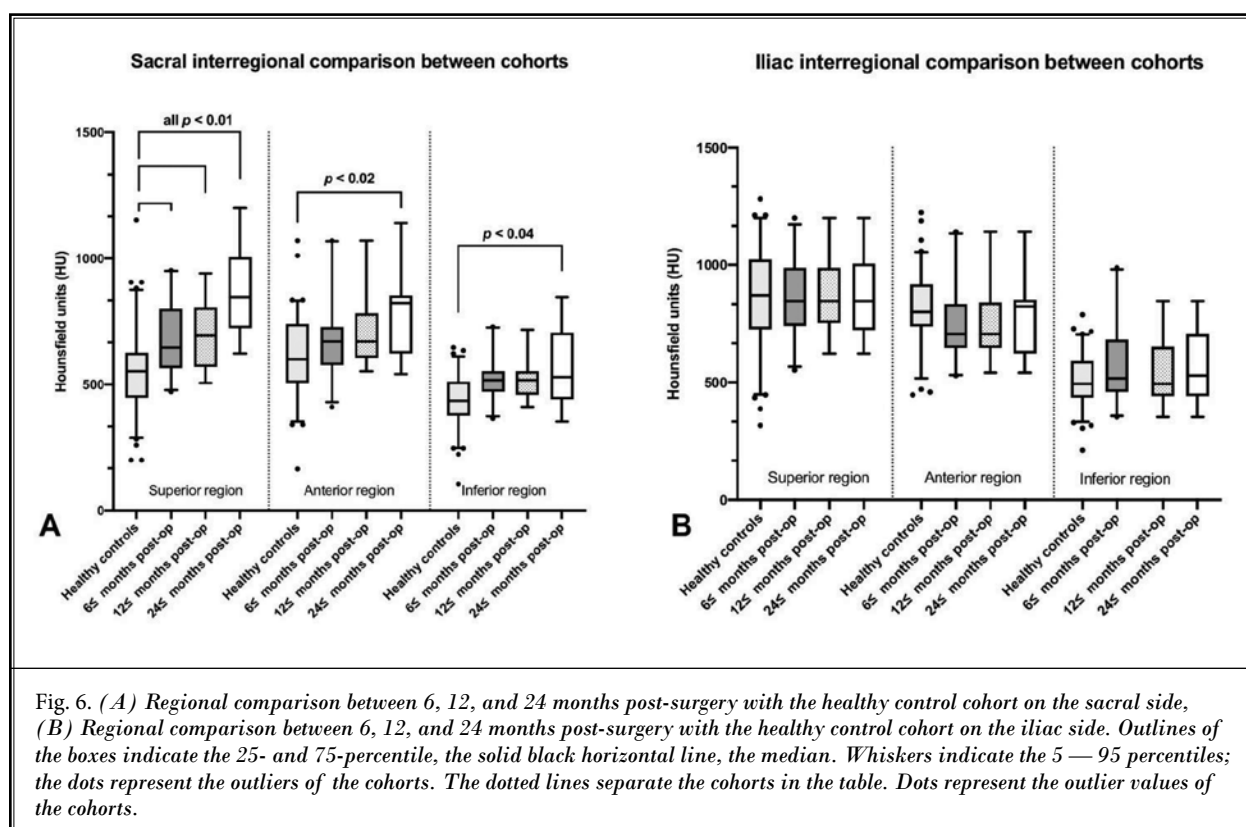


changes in the mechanical stresses after fusion of the joint. Furthermore, the study compared mineralization patterns of patients having undergone SIJ arthrodesis with healthy controls to determine whether pathology-related alterations in the SIJ subchondral bone density normalize back to a healthy pain-free condition.

Sacroiliac Arthrodesis Results in an Increasing Morpho-Mechanical Conformity within the SIJ

Usually a little SIJ motion is useful to dissipate the load to the surrounding areas (i.e., the musculature, cartilage, and ligaments [27]). In the surgically-fused SIJ, the range of motion decreases (9) and loads could be applied to larger areas of the sacrum and the ilium instead of the surrounding structures. As a result of SIJ arthrodesis, a higher load would be transferred via the bony SIJ. Therefore, subchondral bone mineralization of

the SIJ could be altered. As a consequence of the altered biomechanics, initially significant in the superior part (most likely due to the surgical method), the entire joint is affected resulting in the pattern to gradually become more uniform over time. Ultimately, we could assume that this is a compensatory mechanism in response to the new loading situation. This increase might continue to evolve after 4 years (this would have to be verified) or it may represent a new mineralization state of the joint. The stresses are transferred in a more uniform bone-to-bone manner which is here reflected with a clear trend towards conformity between the sacrum and ilium, specifically in the inferior and anterior regions. On the sacral side, subchondral bone mineralization increased. It means that loads could be compensated mainly on the sacral side rather than the ilium side. In this scenario, our first hypothesis can be accepted as there is a trend towards conformity in the SIJ after fusion.



Bone Mineral Density of the Sacrum Increases Following Surgical Joint Fusion

A previous study provided first insights into the mineralization pattern distribution in healthy controls and SIJD-affected patients. It was found that SIJD joints showed signs of increased density in the inferior sacral region resulting from mechanically induced stresses in the subchondral bone plate (26). When comparing SIJD-affected joints with those surgically fused, increased density was found in all sacral regions in the post-operative state. Therefore, our second hypothesis stating that subchondral bone density increases as a result of SIJ arthrodesis can be accepted, however, only on the sacral side but not on the iliac side. There was a trend towards increased density, but there was only a significant difference in the superior portion of the joint 6 months post-surgery compared to 12 and 24 months. These findings may reflect the alteration in the joint kinematics of the SIJ due to the SIJ arthrodesis. The temporary mineralization difference in the superior sacral region may be related to an increase in forces caused by the sudden change in dynamics caused by the surgical procedures including bone grafting in this region. However, localized bone

grafting within the joint cavity is likely not responsible for an increase in mineralization on a particular bone side (i.e., sacrum) but is more prone to affect the bone complex in the region where bone was grafted for the intervention.

Furthermore, comparison between each region at each time point post-operatively showed no significant differences which speaks in favor of a simultaneous mineralization with the same velocity. These forces reflect the continuous adaptation of the surface to the differences in applied loads which may also relate to the surgical technique applied. In fact, HU values appear to respond (being significantly different from the normal baseline) quicker within the first 6 months in areas where the biomechanics strongly differ from the healthy state; i.e., the superior region is largely affected by the implant placement in most surgical techniques (28). This included the most common procedures used in this study: the anterior and posterior approaches. Bone grafting was performed in the superior part of the SIJ after curettage of the subchondral area in the anterior approach and cylinder cages were inserted around the superior part of the SIJ in the posterior approach (5).

Surgically treated Joints Reflect Variable Morpho-mechanical Density Patterns When Compared to Healthy Joints

Pain-relief is the main objective when fusing the SIJ in SIJD patients. Regarding the relationship between pain and altered bone density within the SIJ, 3 mechanisms are hypothesized for understanding the results of this study. Firstly, bone mineralization changes within the painful SIJ cause the pain to progress within the joint. This would mean both phenomena are correlated which creates a vicious circle of cause-and-effect between increased mineralization and pain. Secondly, the ligamentous failure and laxity around the SIJ causes partial incompetence of the joint causing morpho-mechanical alterations to the SIJ surface manifesting itself as a hyper-mineralization within the zones of incompetence. The results of this study could support the last hypothesis. Finally, ligament laxity causing SIJD results in compensatory mechanisms to take over to compensate for abnormal loading and stresses which puts the SIJ under active compression. This would have the consequence of altering the subchondral bone density of the auricular surfaces.

In normal pelvic kinematics, the sacrum is suspended between the ligaments and muscles of the posterior pelvis (29). The primary aim of SIJ arthrodesis is to relieve pain of the SIJ by immobilizing the joint within the pelvis. This may have the effect of relieving peak loads to the surrounding SIJ areas which are filled with pain receptors (30). This immobilization of the sacrum between the ilia unavoidably alters the load transmission within the pelvis, which has the consequence of altering the density within the subchondral bone over time. Our third hypothesis stating that the mineralization pattern of the auricular SIJ surface remains different when compared to a healthy cohort can be accepted on the sacral side. The changes in load transmission were reflected here as a mineralization increased in the superior region 6 months post-operatively and progressed into all 3 sacral regions, visible after 12 and 24 months post-operatively.

Additionally, it was found that the superior sacral region shows immediate significant differences as the surgical technique alters this region directly (placement of screws). The other 2 regions respond to the altered biomechanical state with an increased mineralization that becomes significant after 12 and 24 months compared to the healthy controls. From these results, we could hypothesize the following: mineralization appears to respond quicker (within 6 months to a year)

in areas where the biomechanics strongly differ from the healthy state (i.e., the superior region) depending on the surgical approach than in the other regions which only show significant changes after 12 and 24 months compared to the healthy state. The most important finding of this study was that anterior and inferior sacral regions showed higher mineralization than healthy joints at 12 and 24 months follow-up groups. It would be a useful visible change in biomechanics due to the SIJ arthrodesis. Physicians can know the change of SIJ biomechanics due to SIJ dysfunction, which may occur 2 years prior, according to increasing bone density in the anterior and inferior region of the sacrum.

The consequence is that a significantly altered mineralization pattern in patients with SIJD who have not undergone surgery could be caused by either large biomechanical changes occurring within a comparatively short period of time or a gradual adoption of a mineralization pattern caused by biomechanical changes which minutely differ from the healthy state. This could be useful information clinically, as it would allow the detection of misalignment or dysfunction in the SIJ in response to altered loading-conditions depending on how fast the mineralization occurs.

Limitations

The given study is limited in sample size. Post-operative CT scans had screws which may have left artifacts or partial volume effects on the surfaces. Though clearly patterns were observed for the sacrum but not the ilium, a bias may remain. Healthy controls were different patients to the SIJD and post-operative cohorts, comparison was made as both cohorts were age matched; however, this comparison did not take into account potential population differences. Size differences in the regions may have also been an influencing factor of the results as the regions were based on the size and shape of the articular surface. Future studies in larger sample sizes should also make an attempt to quantify potential differences in the surgical approach chosen and the implant being used.

CONCLUSIONS

Altered stresses and loads caused by the immobilization of the SIJ after arthrodesis results in an increase in mineral density in the sacral auricular surface manifesting as an increased morpho-mechanical conformity in the anterior and inferior regions. Furthermore, surgically treated joints reflect variable morpho-mechanical density patterns when compared

to healthy joints resulting from the permanent changes in pelvic dynamics. Alterations in mineralization may be related to the surgical approach and screw placement, which provides time-related information on the overall appearance of the SIJ and its state of

dysfunction. This novel study provides a foundation to establish cut-off HU values using larger cohorts in the future and provides fundamental data for an objective morphological correlation of altered pain-related pelvic biomechanics.

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Subchondral Bone Density Alterations Following Sacroiliac Joint Arthrodesis

Supplemental Table 1. Mean HU values of the cohorts and conformity between iliac and sacral sides.

Category	Bone	Pre-operative vs. 6 months post-op (n = 23)*			Pre-operative vs. 12 months post-op (n = 17)*			Pre-operative vs. 24 months post (n = 13)*		
		Superior region	Anterior region	Inferior region	Superior region	Anterior region	Inferior region	Superior region	Anterior region	Inferior region
Pre-operative	Sacrum	581 ± 179	662 ± 176	516 ± 109	602 ± 195	680 ± 167	518 ± 113	580 ± 205	667 ± 171	520 ± 109
	Ilium	893 ± 214	760 ± 165	550 ± 144	932 ± 205	764 ± 144	535 ± 126	923 ± 175	759 ± 144	531 ± 118
	P values	P < 0.01*	P > 0.1	P > 0.4	P < 0.01*	P > 0.1	P > 0.8	P < 0.01*	P > 0.1	P > 0.8
Post-operative	Sacrum	670 ± 142	689 ± 165	520 ± 88	688 ± 130	717 ± 161	519 ± 77	703 ± 132	734 ± 179	536 ± 79
	Ilium	851 ± 160	756 ± 163	571 ± 175	863 ± 157	756 ± 171	539 ± 142	864 ± 174	781 ± 190	558 ± 154
	P values	P < 0.01*	P > 0.2	P > 0.3	P < 0.01*	P > 0.6	P > 0.7	P < 0.01*	P > 0.1	P > 0.8
Category	Bone	Superior region	Anterior region	Inferior region						
Healthy controls (n = 78)	Sacrum	541 ± 136	618 ± 159	447 ± 91						
	Ilium	868 ± 211	825 ± 121	509 ± 114						
	P values	P < 0.01*	P < 0.01*	P < 0.03*						

*mean values of the preoperative cohort and SD change as a consequence of removing datasets following matched paired analyses. The P value represents statistical significance at < 0.05 in bold.

Supplemental Table 2. Comparison between the cohorts of each region per bone and region at each time-point.

Category	Bone	6 months post-op (n = 24)			12 months post-op (n = 17)			24 months post (n = 13)		
		Superior region	Anterior region	Inferior region	Superior region	Anterior region	Inferior region	Superior region	Anterior region	Inferior region
Pre-operative vs. post-operative joints	Sacrum	P < 0.02*	P > 0.4	P > 0.8	P > 0.2	P > 0.4	P > 0.9	P > 0.1	P > 0.2	P > 0.6
	Ilium	P > 0.9	P > 0.9	P > 0.6	P > 0.8	P > 0.8	P > 0.8	P > 0.4	P > 0.7	P > 0.4
Post-operative vs. healthy joints	Sacrum	P < 0.01*	P > 0.1	P > 0.1	P < 0.01*	P > 0.1	P > 0.1	P < 0.01*	P < 0.02*	P < 0.04*
	Ilium	P > 0.8	P > 0.2	P > 0.3	P > 0.9	P > 0.2	P > 0.7	P > 0.9	P > 0.4	P > 0.5

The P value represents statistical significance at < 0.05 in bold.