British Medical Bulletin, 2025, **153**, 1–10
https://doi.org/10.1093/bmb/ldae023
Invited Review

Safety and performance of a novel synthetic biomimetic scaffold for iliac crest defect reconstruction during surgical treatment of pelvic girdle pain: a first-in-human trial

Peter V. Giannoudis[1,2], Paul Andrzejwski[1], George Chloros[1], Elizabeth M.A. Hensor[2]

[1]Academic Department of Trauma & Orthopaedics, School of Medicine, University of Leeds, Leeds, UK
[2]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, UK

*Corresponding author: Peter Giannoudis, Professor & Chairman of Trauma and Orthopaedics, Academic Department of Trauma & Orthopaedic Surgery School of Medicine, University of Leeds, Leeds, UK. Email: pgiannoudi@aol.com, p.giannoudis@leeds.ac.uk

Abstract

Introduction: Surgical treatment of pelvic girdle pain (PGP) involves arthrodesis of sacroiliac (SI) and pubic symphysis joints. Fusion of pubic symphysis involves the implantation of an autologous iliac crest tricortical graft harvested from the iliac crest. The objective was to assess the safety of a novel synthetic graft substitute (b.Bone) for iliac crest reconstruction and to evaluate the results of PGP surgical treatment.

Sources of data: Consecutive participants undergoing pelvic fusion and requiring iliac crest reconstruction were enrolled and followed-up for 12 months in a prospective first-in-human clinical investigation. Adverse events were documented, and health-related quality of life was evaluated using EuroQol-5D-5L questionnaire. Iliac crest defect healing was evaluated by the Modified Lane and Sandhu radiological scoring system. In addition, relevant published peer-reviewed scientific articles identified from PubMed.

Areas of agreement: The EQ-5D-5L scores improved steadily reaching the highest point at 365 days. By 365 days complete healing of the bone defect was observed.

Areas of controversy: The management of PGP remains challenging with mixed results reported in the literature.

Growing points: While there is lack of consensus on how to manage PGP, the present study shows improved outcomes at one year following surgery. The synthetic b.Bone scaffold is a safe option with good healing outcomes for iliac crest defect reconstruction.

Areas timely for developing research: Although b.Bone synthetic scaffold found to be safe, further studies reporting on surgical treatment of PGP are required to confirm the findings in comparative trials.

Keywords: pelvic pain; hypermobility; pelvic fusion; b.Bone scaffold.

Level of evidence: Therapeutic level phase 0

Introduction

Pelvic girdle pain (PGP) refers to pain localised over the posterior iliac crest, gluteal fold, and the anterior and posterior aspects of the pelvic ring in general.[1] Etiological factors associated with the development of PGP include lumbar spine disorders, trauma, pregnancy, and hypermobility syndrome amongst others.[2] The true incidence of joint hypermobility remains unknown but recent epidemiological studies estimated the prevalence to be between 2% and 57%.[3,4,5]

Joint hypermobility is associated with amplified elasticity of the surrounding soft tissues, ligaments and tendons supporting a joint, leading to a wider range of movement. This increased 'abnormal' movement may induce joint instability, painful stimuli and activity restrictions affecting activities of daily living and

Received 25 October 2024; **Revised** 5 December 2024; **Accepted** 13 December 2024

quality of life. The pain generated is believed to be secondary to the altered biomechanics directly impacting the transmission forces and physiological function of the anterior and posterior joints (pubic symphysis; sacroiliac [SI] joints) of the pelvic ring. Abnormal overload of the joints leads to recurring microtrauma, chronic inflammatory conditions and gradual cartilage degeneration with the end product being 'osteoarthritis'.

Management of PGP can be non-operative or surgical. No-operative treatment includes medication, pelvic floor exercises, lower lumbar spine physical therapy, acupuncture, radiofrequency, and injections.[6] Surgical treatment involves fusion of the SI joints posteriorly and/or pubic symphysis anteriorly. Open and minimally invasive techniques have been described in the literature, but few studies have evaluated the results.[7–9] For fusion of the pubis symphysis, one technique involves harvesting of an autologous tricortical graft from the iliac crest implanted at the bed of pubic symphysis followed by osteosynthesis of the pubic joint.[10] The iliac crest defect created is then reconstructed with allograft, xenograft or with mesh related materials.[11]

The objectives of this study were to investigate the safety and performance of a synthetic scaffold (b.Bone)[12,13] used to reconstruct the iliac crest bone defect created during surgical fusion of the pubic symphysis joint, and to evaluate the results of pelvic fusion in patients with PGP.

Materials and methods

Study design

This was a prospective, open-label, single-arm, first-in-human clinical investigation. Inclusion criteria were male or female participants, aged 18–70 years, undergoing pelvic fusion due to PGP and requiring iliac crest reconstruction, and ability to provide informed consent. Exclusion criteria were presence of infection, bone malignant tumor, treatment with chemotherapy or radiotherapy within 12 months before enrolment, known inflammatory systemic diseases, coagulopathy or bleeding disorders, treatment with systemic immunosuppressive agents, including steroids, and known or suspected allergy or hypersensitivity to the b.Bone implant components. Pregnant women and/or women that intended to be pregnant within 6 or 12 months from surgery were also excluded.

PGP pain was diagnosed using pain provocation tests. The anterior aspect of the pelvic ring was examined with deep palpation of the pubic symphysis and the modified Trendelenburg's test.[1] We screened for hypermobility syndrome using the Beighton score.[14]

Radiographic investigations included magnetic resonance imaging (MRI) and plain radiographs assessing pelvic instability by acquiring alternating single-leg stance (flamingo view) images, which can demonstrate significant pubis translation.[15]

All participants had failed ≥12 months of conservative treatment (oral analgesia, physiotherapy, local corticosteroid injections).

Regulatory and Independent Ethical Committee approval (IRAS 246763) was obtained for the site before initiation. The study was conducted in accordance with the Declaration of Helsinki (1964), amended Japan (1975), Italy (1983), Hong Kong (1989), Republic of South Africa (1996), Scotland (2000), Brazil, (2013), and Good Clinical Practice (1996) and was registered in ClinicalTrials.gov (NCT03836404).

Description of b.Bone scaffold

b.Bone is a synthetic, acellular, 3D porous hydroxyapatite scaffold that is produced using a biomorphic transformation of a natural wood (rattan wood). It consists of wide channels (pores) ∼300 μm and other smaller connected tubules mirroring the microstructure and mechanical stiffness of the cortical bone. b.Bone is prepared by supporting the dissolution of calcite and re-precipitation of HA-nanocrystals of ∼20 nm in thickness and ∼150 nm in width being loaded with Mg^{2+} and Sr^{2+} ions for improved biocompatibility and bone formation.[12,13]

Sample size

The sample size (n = 15) was chosen to be consistent with first-in-human studies of pharmacological agents.[16] Safety was reviewed after the first five participants had been treated. If there were no complications observed, using 1-alpha1/n[17] we would have had 82% confidence that the risk was below 0.29 (the reported overall complication rate for standard care).[18] The best estimate for the risk, based on 2/5n,[19] would be 0.08, consistent with the reported rate of major complication in standard care.[20]

Study interventions

Fusion of the pelvic ring (SI joints and pubis symphysis) was performed based on the affected joints and symptom severity.

For the fusion of the pubic symphysis, a Pfannenstiel approach was used. The pubic cartilage was excised and a 3 cm tricortical graft, harvested from the iliac crest, was placed in the pubic symphysis joint to facilitate fusion followed by stabilisation of the joint with an 8-hole 3.5 mm reconstruction plate.

Sacroiliac joint fusion used the minimal invasive arthrodesis i-fuse implant system as previously described.[21,22] For each joint, two implants were used (S1 and S2 bodies respectively). During all procedures the participant was supine on a radiolucent table (OSI).

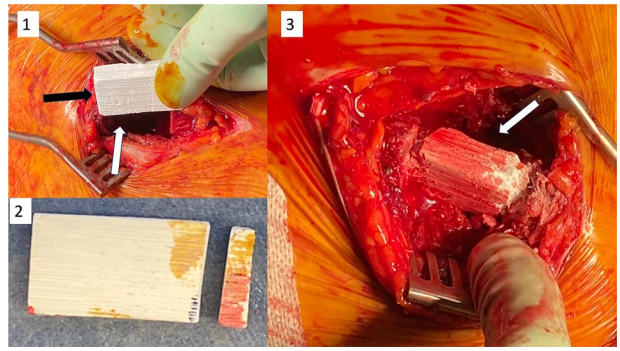

Figure 1. Intra-operative picture of iliac crest defect reconstruction with b.Bone scaffold. 1.White arrow pointing to iliac crest defect; black arrow pointing to b.Bone scaffold. 2. b.Bone scaffold cut to size to fit in the iliac crest defect area with electric saw. 3. White arrow showing the press fit implantation of the b.Bone scaffold within the iliac crest defect area.

At induction, participants received antibiotic prophylaxis (flucloxacillin 1gr and gentamycin 500 mg). Postoperatively, participants received chemical thromboprophylaxis for a period of 10 weeks (tinzaparin 4500 IU, once a day). All participants refrained from full weightbearing and mobilised using a wheelchair for 10 weeks, initiating an active physical therapy rehabilitation program thereafter.

The 3 cm iliac crest defect created when harvesting the autologous tricortical graft was reconstructed with a press fit technique using the b.Bone scaffold (Fig. 1). b.Bone is a ceramic re-absorbable scaffold engineered to reflect anatomical and physiological bone hierarchical structures.

It is made of biomimetic substituted calcium phosphate phases (HA + β-TCP and ions).[12,13]

Following discharge from the hospital participants visited the orthopaedic outpatient clinic for clinical and radiological assessments at 1, 3, 6, and 12 months.

Health-related quality of life was assessed using the EuroQol-5D-5L questionnaire and a visual analogue score (VAS) to assess the severity of pain (0-10 cm; 10 being the worst pain).

Adverse events were documented and classified according to the Clavien-Dindo criteria.[23]

Radiographic assessments

X-rays were obtained at every visit; if radiological healing could not be verified by plain radiographs a pelvic CT was requested.

Defect healing was evaluated using by Modified Lane and Sandhu radiological scoring system (MLS).[24]

Safety monitoring

An independent Data Safety Monitoring Board (DSMB) consisting of five independent experts reviewed the safety data during the trial.

Statistical analysis

Descriptive analyses were performed using appropriate descriptive statistics (mean, standard deviation, median, 1st & 3rd quartiles, and range for continuous variables, and frequencies and percentages for categorical variables). EQ-5D-5L index scores were calculated via a cross-walk to the UK EQ-5D-3L time trade-off value set. A range of upper confidence limits (75%, 80%, 85%, 90%, 95%, 99%) for the major and minor complication rates were calculated. If 9/15 participants experienced minor or major complications, or if 4/15 experienced major complications, this would indicate with 95% confidence that the rates in participants receiving the experimental treatment exceeded the reported rates for standard care.

Results

Study population

Of the 15 participants enrolled and treated, one was discontinued from the trial as the b.Bone implant was removed after 26 days of implantation (participant had a fall due to a non-epileptic seizure that led to the implant migrating from the iliac crest defect), Fig. 2.

Participant baseline characteristics are presented in Table 1.

Sacroiliac joint fusion

At 12 month follow up there was no radiological evidence of i-fuse implant displacement or failure. The majority of implants demonstrated bone apposition to the implants (on sacral and iliac sides of the joint). Not in every case intra-articular fusion with bridging of trabeculae from ilium to sacrum was detected.

Pubic symphysis fusion

Radiological evaluation demonstrated fusion in all participants, Fig. 3.

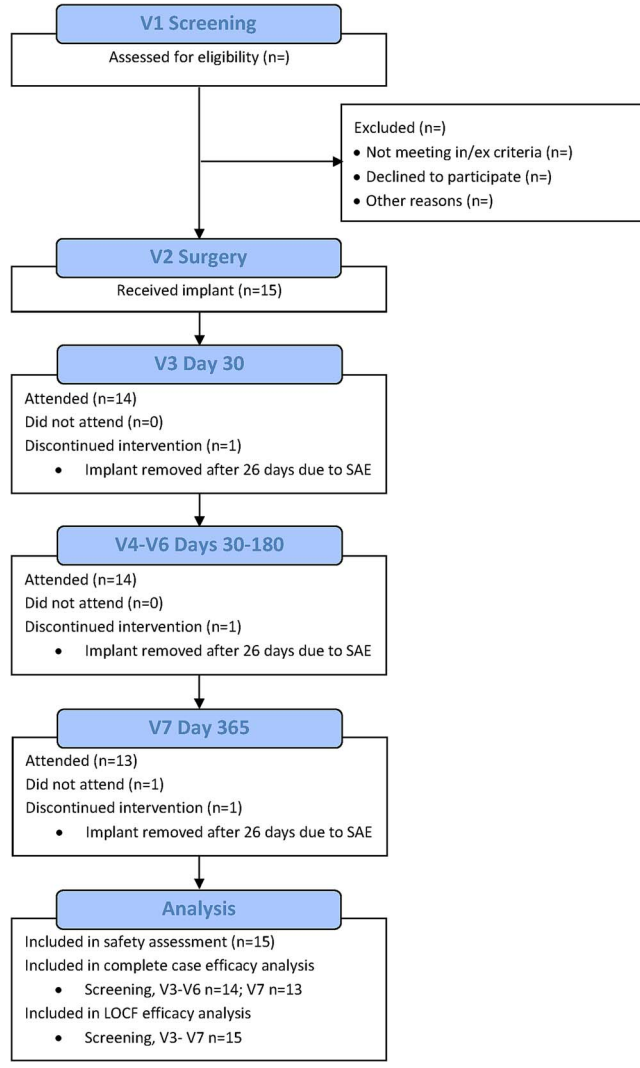

Figure 2. Consolidated standards of reporting trials (CONSORT) flow diagram of the study.

Analysis of adverse events

There were 34 adverse events in 14 participants, 10 of which, in five participants, were deemed to be serious. Adverse events are summarised in Table 2.

Overall, four events were considered to be related to the device and/or graft site. Three were minor complications; two superficial wound infections to the iliac graft site, and one instance of indentation at the graft site that was deemed to be related to both the device and the graft site, all of which resolved.

The numbers of participants experiencing device- and/or graft site-related complications were well below the pre-specified thresholds that would have indicated that the rates in participants receiving the b.Bone implant exceeded the rates reported by Younger and Chapman for standard care.[16] These thresholds were n = 9/15 for minor or major complication (cf. n = 4/15 observed) and n = 4/15 for major complications (cf. n = 1/15 observed). The upper bounds of the confidence intervals around the proportions of participants experiencing complications ranged between 33.8% (75% CI) and 54.3% (99% CI) for minor or major device- or iliac graft site-related complications, and between 9.6% and 26.8% for major device- or iliac graft site-related complications.

Serious adverse events

In the cohort included in this study, 10 SAEs were documented, half of them (five SAEs) occurring in one participant with a background of non-epileptic seizures,

Table 1. Patient demographics.

Characteristic	Number of Patients	Summary
Female/Male	15	14/1
Age (median, IQR), range years	15	46 (39 to 55), 25–65
Ethnicity White/Other	15	14/1
Current Smoker	15	2 (13.3%)
Hypermobility n (%)	15	9 (60%)
Years with symptoms mean (SD), range	15	9.8 (range 4–20)
Prior Non-operative treatment	15	15 -Pain relief Medication -Physical Therapy -Injections
History of previous surgery (arthrodesis)	15	No
SI Joint fusion (Bilateral)	14	11
SI Joint Unilateral		3
Pubic symphysis Fusion	15	15

Table 2. All adverse events recorded.

	All events		
	AE N = 24	SAE N = 10	Total N = 34
Total number of AEs	24	10	34
Number of unique events (recurring counted once)	23	7	30
System Order Class			
General disorders and administration site conditions	1 (4.2%)	0 (0.0%)	1 (2.9%)
Immune system disorders	1 (4.2%)	0 (0.0%)	1 (2.9%)
*Infections and infestations	9 (37.5%)	0 (0.0%)	9 (26.5%)
Injury, poisoning and procedural complications	2 (8.3%)	1 (10.0%)	3 (8.8%)
Musculoskeletal and connective tissue disorders	6 (25.0%)	1 (10.0%)	7 (20.6%)
Nervous system disorders	2 (8.3%)	1 (10.0%)	3 (8.8%)
Renal and urinary disorders	1 (4.2%)	0 (0.0%)	1 (2.9%)
Reproductive system and breast disorders	1 (4.2%)	0 (0.0%)	1 (2.9%)
Respiratory, thoracic and mediastinal disorders	0 (0.0%)	1 (10.0%)	1 (2.9%)
Surgical and medical procedures	1 (4.2%)	5 (50.0%)	6 (17.6%)
Vascular disorders	0 (0.0%)	1 (10.0%)	1 (2.9%)
Clavien-Dindo classification			
Grade 1	13 (59.1%)	1 (10.0%)	14 (43.8%)
Grade 2	6 (27.3%)	2 (20.0%)	8 (25.0%)
Grade 3a	2 (9.1%)	0 (0.0%)	2 (6.3%)
Grade 3b	0 (0.0%)	7 (70.0%)	7 (21.9%)
Not answered	1 (4.5%)	0 (0.0%)	1 (3.1%)
Intensity			
Mild	23 (95.8%)	0 (0.0%)	23 (67.6%)
Moderate	1 (4.2%)	9 (90.0%)	10 (29.4%)
Severe	0 (0.0%)	1 (10.0%)	1 (2.9%)
Relatedness			
Related to device	1 (4.2%)	0 (0.0%)	1 (2.9%)
Related to iliac graft site	3 (12.5%)	1 (10.0%)	4 (11.8%)
Related to device and/or iliac graft site	3 (12.5%)	1 (10.0%)	4 (11.8%)

*Includes: eye infection, covid-19, UTI (urinary tract infection), cellulitis.

all of them being unrelated to the b.Bone device (participant developed pubic symphysis infection requiring several trips to the operating theatre for irrigation and debridement of the pubic surgical wound).

The other five SAEs occurring in four participants being inguinal hernia, revision of SI joint pin position, drowsiness, pulmonary embolism (PE) and a urinary bladder tear, were all complications that could occur

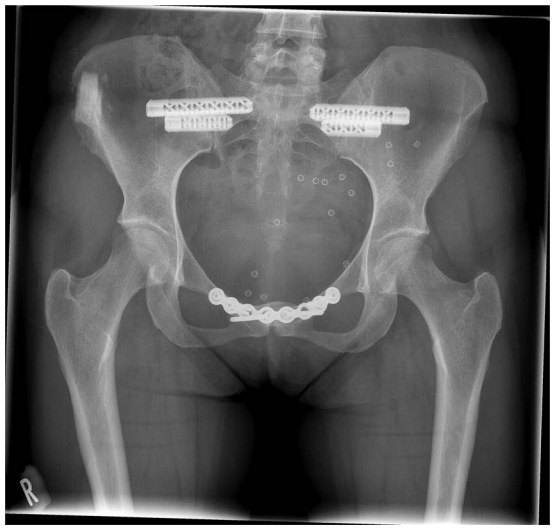

Figure 3. AP pelvic radiograph showing fusion of the pubic symphysis at 6 months follow up.

following this type of surgery and all were unrelated to the b.Bone implant.

The upper bounds of the confidence interval around the proportion of participants experiencing an SAE ranged from 45.4% (75% CI) to 66.0% (95% CI).

Overall, no serious adverse events were documented related to the pelvic iliac crest graft site other than the removal of one device that was displaced following a fall, shortly after implantation, in a participant with a non-epileptic seizure, which was deemed a major complication. No issues were observed in relation to allergic reactions or rejection of the b.Bone device.

Deaths

There were no deaths during the trial.

Bone regeneration

Bone regeneration of the iliac crest defect following the implantation of the b.Bone scaffold was assessed at 1, 30, 60, 90, 180, and 365 days. Due to the removal of one implant which was displaced following a non-epileptic seizure, the degree and rate of bone regeneration was evaluated in 14 participants. The first radiological signs of healing were observed at 60 days when the median MLS score was 5/10 (range 2–7). By 90 days and 180 days the score increased to median (range) 6 (3–8) and 7.5 (5–10), respectively. By 365 days complete healing of the defect was noted in 12/14 (median 10; range 8–10), Fig. 4. There were no cases of defect non-union or implant failure to progress to integration within the host environment, Fig. 5.

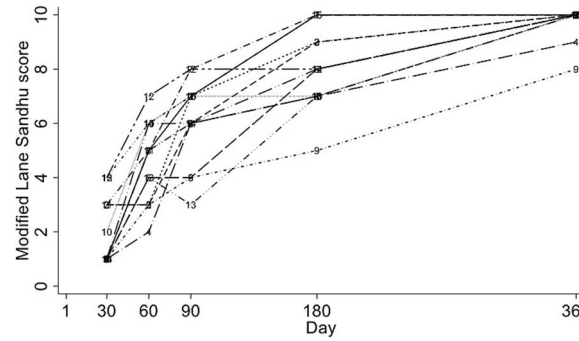

Figure 4. Iliac crest defect bone healing assessed by the modified Lane Sandhu score.

EQ-5D-5L index score, visual analogue scale, dimension scores

The EQ-5D-5L index score, where a score of 1 indicates perfect health, was low at baseline (mean [SD] 0.308 [0.215]). Post-baseline EQ-5D-5L outcomes were collected in 14 participants, due to one participant being excluded, but another participant did not fully complete all items at some visits. Immediately after surgery index scores went down. However, after the 60-day point of assessment (mean [SD] -0.052 [0.107], n = 13) the index score was found to be increasing steadily over the subsequent time points of assessment reaching the highest point at 365 days (0.696 [0.250], n = 13). EQ-5D-5L VAS scores followed a similar pattern (data not shown). Dimension scores are presented in Table 3.

Participant-reported pain: VAS (cm)

Post-baseline visual analogue pain scores, where 10 represents the worst pain, were collected from 14 participants. The VAS score demonstrated a downward trend throughout the study period of the trial, from a median (1st quartile, 3rd quartile) of 6 (5, 8) at day 1 to 2 (1, 3) at day 365, Fig. 6.

Number of re-interventions

Apart from the one case (1/15; 6.7%) where the b.Bone implant was removed due to displacement from the iliac crest defect site following a fall, no re-interventions were carried out in relation to the b.Bone implant.

Discussion

In this first-in-human trial a synthetic bone substitute (b.Bone) was used to reconstruct the iliac bone defect caused during pelvic fusion for treatment of PGP. With its inherent physical and biomimic properties, possessing similar structural properties to bone, the device was found to be user-friendly and integrated well with the host environment. There were no adverse events in

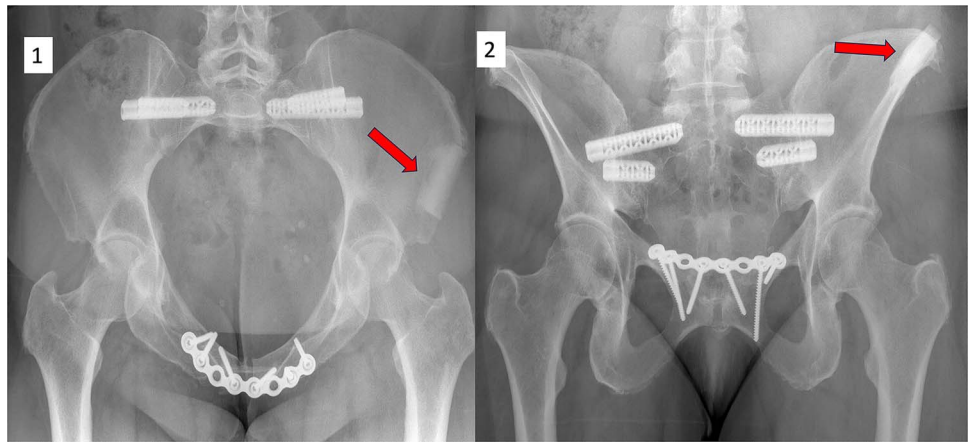

Figure 5. Radiographs of pelvis at 12 month follow up. 1. Inlet view; 2. outlet view; red arrows pointing at the iliac defect showing full integration of the b.Bone scaffold.

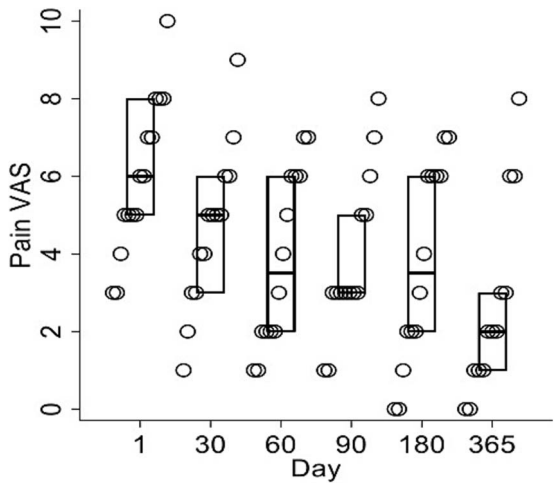

Figure 6. Boxplot of pain VAS during the 12 month follow up time.

relation to its integration with the bone of the host since no inflammation episodes were observed. The anatomical continuity of the crest was noted to be restored in all participants, who reported satisfaction in terms of the local cosmesis (data not shown). Moreover, by the 6 and 12 month follow up time point complete healing in terms of bone regeneration was observed.

Surgical treatment of PGP consisted of arthrodesis of SI and pubis symphysis joints. All participants had a prolonged period of conservative treatment prior to being offered surgery. The mean symptom duration was 9.8 years (4–20). Interestingly, the majority of participants (60%) had been diagnosed with hypermobility syndrome, in which the increased soft tissue flexibility, impaired proprioception, poor coordination and altered biomechanics affecting the lumbopelvic movements can lead to pelvic instability and chronic symptomatology.[25] All participants underwent diagnostic joint injections prior to arthrodesis.

Kibsgård et al. assessed in a prospective study the outcome of surgical treatment in people with PGP. The authors reported improved outcomes using the Oswestry Disability Index (ODI), Short Form-36 (SF-36) and pain VAS scores. Using an anterior approach to the SIJ, complications recorded included infection, complex regional pain syndrome associated with foot drop and loss of bladder sensation.[26]

SIJ arthrodesis can be performed either with open or minimally invasive techniques. Due to the increased risk of complications, lately a minimal invasive approach has gained popularity. Several minimal invasive implants exist including hydroxylapatite screws, hollow modular anchorage screws and triangular titanium implants. In a recent metanalysis carried out evaluating the effect of minimally invasive surgery on VAS and ODI it was found improved outcomes in those treated with these minimal invasive procedures.[27] For the arthrodesis of the pubic symphysis an open technique previously described was used successfully in all participants.[10] The tricortical graft harvested from the iliac crest was well incorporated facilitating fusion of the pubic symphysis joint in all cases.

In this study triangular titanium implants were used for the SIJ arthrodesis. A review of this method by the National Institute for Health and Care Excellence in the UK concluded that there is evidence that improved pain, ODI, and quality of life outcomes for the management of chronic SIJ pain can be expected.[28]

The functional scores we obtained relating to health quality of life and pain scores showed improvement throughout the study period. By 12 months the EQ-5D-5L and pain VAS scores were better compared to the

Table 3. EQ-5D-5L dimension scores.

	Day					
	1 N = 15	**30** N = 15	**60** N = 15	**90** N = 15	**180** N = 15	**365** N = 15
Mobility						
I have no problems in walking about	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (6.7%)	5 (33.3%)
I have slight problems in walking about	2 (13.3%)	0 (0.0%)	0 (0.0%)	3 (20.0%)	5 (33.3%)	3 (20.0%)
I have moderate problems in walking about	6 (40.0%)	0 (0.0%)	0 (0.0%)	3 (20.0%)	5 (33.3%)	4 (26.7%)
I have severe problems in walking about	7 (46.7%)	0 (0.0%)	0 (0.0%)	1 (6.7%)	3 (20.0%)	1 (6.7%)
I am unable to walk about	0 (0.0%)	14 (93.3%)	14 (93.3%)	6 (40.0%)	0 (0.0%)	0 (0.0%)
Missing	0 (0.0%)	1 (6.7%)	1 (6.7%)	2 (13.3%)	1 (6.7%)	2 (13.3%)
SelfCare						
I have no problems washing or dressing myself	4 (26.7%)	0 (0.0%)	2 (13.3%)	2 (13.3%)	4 (26.7%)	8 (53.3%)
I have slight problems washing or dressing myself	6 (40.0%)	5 (33.3%)	3 (20.0%)	4 (26.7%)	4 (26.7%)	3 (20.0%)
I have moderate problems washing or dressing myself	4 (26.7%)	7 (46.7%)	4 (26.7%)	3 (20.0%)	5 (33.3%)	1 (6.7%)
I have severe problems washing or dressing myself	1 (6.7%)	2 (13.3%)	4 (26.7%)	3 (20.0%)	1 (6.7%)	1 (6.7%)
I am unable to wash or dress myself	0 (0.0%)	0 (0.0%)	1 (6.7%)	1 (6.7%)	0 (0.0%)	0 (0.0%)
Missing	0 (0.0%)	1 (6.7%)	1 (6.7%)	2 (13.3%)	1 (6.7%)	2 (13.3%)
Usual						
I have no problems doing my usual activities	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (6.7%)	5 (33.3%)
I have slight problems doing my usual activities	1 (6.7%)	0 (0.0%)	0 (0.0%)	2 (13.3%)	5 (33.3%)	3 (20.0%)
I have moderate problems doing my usual activities	7 (46.7%)	2 (13.3%)	3 (20.0%)	5 (33.3%)	2 (13.3%)	3 (20.0%)
I have severe problems doing my usual activities	6 (40.0%)	3 (20.0%)	4 (26.7%)	1 (6.7%)	4 (26.7%)	2 (13.3%)
I am unable to do my usual activities	1 (6.7%)	9 (60.0%)	7 (46.7%)	5 (33.3%)	2 (13.3%)	0 (0.0%)
Missing	0 (0.0%)	1 (6.7%)	1 (6.7%)	2 (13.3%)	1 (6.7%)	2 (13.3%)
Pain						
I have no pain or discomfort	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (6.7%)	3 (20.0%)
I have slight pain or discomfort	0 (0.0%)	5 (33.3%)	5 (33.3%)	5 (33.3%)	4 (26.7%)	6 (40.0%)
I have moderate pain or discomfort	6 (40.0%)	5 (33.3%)	4 (26.7%)	5 (33.3%)	6 (40.0%)	2 (13.3%)
I have severe pain or discomfort	6 (40.0%)	4 (26.7%)	4 (26.7%)	3 (20.0%)	3 (20.0%)	2 (13.3%)
I have extreme pain or discomfort	2 (13.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Missing	1 (6.7%)	1 (6.7%)	2 (13.3%)	2 (13.3%)	1 (6.7%)	2 (13.3%)
Anxiety						
I am not anxious or depressed	4 (26.7%)	5 (33.3%)	5 (33.3%)	5 (33.3%)	7 (46.7%)	10 (66.7%)
I am slightly anxious or depressed	4 (26.7%)	4 (26.7%)	3 (20.0%)	4 (26.7%)	2 (13.3%)	1 (6.7%)
I am moderately anxious or depressed	4 (26.7%)	4 (26.7%)	4 (26.7%)	4 (26.7%)	4 (26.7%)	2 (13.3%)
I am severely anxious or depressed	2 (13.3%)	1 (6.7%)	1 (6.7%)	0 (0.0%)	1 (6.7%)	0 (0.0%)
I am extremely anxious or depressed	1 (6.7%)	0 (0.0%)	1 (6.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Missing	0 (0.0%)	1 (6.7%)	1 (6.7%)	2 (13.3%)	1 (6.7%)	2 (13.3%)

scores obtained prior to surgery, suggesting a positive impact of surgical intervention.

For the arthrodesis of both the SIJ and pubic symphysis joints full weight bearing was avoided for 10 weeks. This standard protocol (wheelchair for 10 weeks), used in our institution to support integration of the tricortical bone graft anteriorly, may be associated with development of such complications as deep vein thrombosis, PE, muscular wasting and deconditioning and development of skin pressure sores. However, all participants were encouraged to mobilise from bed to wheelchair with a banana board and to do at least twice daily strengthening exercises of the pelvic floor and lower extremities whilst avoiding weight bearing. One participant, despite being on chemical thromboprophylaxis, developed PE that required treatment, which resolved with medical treatment without any long term sequalae. Other adverse events recorded in this study included an inguinal hernia in a participant with hypermobility syndrome, a revision of an i-fuse implant that was causing nerve root irritation, and a urinary bladder tear that was managed with direct repair with an additional suprapubic catheter and resolved 3 weeks after surgery (negative cystogram). All the above complications could occur following this type of surgery.

Harvested tricortical graft blocks from the iliac crest are used to facilitate fusion of joints (i.e. pubis symphysis, SI joint), to structurally support metaphyseal areas of articular impaction injuries (i.e. tibial plateau) and to fill in metaphyseal bone voids. Reconstruction of the iliac defect area can decrease postoperative

pain, haematoma formation, and risk of herniation, minimize functional disability, and improve cosmesis.[29] Different materials have been used for reconstruction of iliac crest defect such as allograft, autogenous ribs, xenograft and bone cement with screws.[30,31] Noteworthy, there has been ongoing research interest to develop and test new biomaterials guiding regeneration of bone and other tissues.[32–34] In this study the b.Bone scaffold provided successfully anatomical continuity of the iliac crest with complete healing of the defect area. This option of defect reconstruction was found to be safe, and it can considered in the surgeon's armamentarium particularly in cases where due to religious or cultural beliefs patients may decline the use of xenograft and allogeneic type of graft materials.

Limitations of this study were the time of follow up (12 months), and the small number of participants. However, for a first-in-human study the number of participants studied is considered adequate.

Strengths included the prospective recruitment of consecutive patients in a single institution, and the review of the safety data by an independent DSMB. In addition, the data collected on the surgical treatment of PGP can inform the design of future larger, prospective randomised trials.

Conclusion

In patients with PGP, the b.Bone synthetic scaffold found to be safe, with positive radiological assessment of defect healing. Our descriptive data suggest that pelvic fusion could improve health related quality of life outcomes and pain scores.

Acknowledgements

We would like to thank Gillian Libby for her contributions to the interim safety analyses for the trial.

Author contributions

Peter Giannoudis: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Writing—original draft, Writing—review & editing; Paul Andrzejowski: Investigation, Resources, Software, Validation, Writing—review & editing; George Chloros: Data curation, Methodology, Software, Supervision, Writing—review & editing; Elisabeth Hensor: Formal analysis, Methodology, Resources, Software, Validation, Writing—review & editing.

Conflict of interest statement

This study was supported from an educational grant (Number 114906) from Greenbone to the University of Leeds.

Funding

Prof P Giannoudis is supported in part by the National Institute for Health and Care Research (NIHR) Leeds Biomedical Research Centre (BRC) (NIHR 203331). The views expressed are those of the author(s) and not necessarily those of the NIHR, or the Department of Health and Social Care.

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

References

1. Vleeming A, Albert HB, Ostgaard HC., *et al.* European guidelines for the diagnosis and treatment of pelvic girdle pain *Eur Spine J*. 2008;**17**:794–819. https://doi.org/10.1007/s00586-008-0602-4.
2. Mulvey MR, Macfarlane GJ, Beasley M., *et al.* Modest association of joint hypermobility with disabling and limiting musculoskeletal pain: Results from a large-scale general population-based survey *Arthritis Care Res*. 2013;**65**:1325–33. https://doi.org/10.1002/acr.21979.
3. Van der Giessen LJ, Liekens D, Rutgers KJ., *et al.* Validation of beighton score and prevalence of connective tissue signs in 773 Dutch children *J Rheumatol*. 2001;**28**:2726–30.
4. Ali A, Andrzejowski P, Kanakaris NK., *et al.* Pelvic girdle pain, hypermobility Spectrum disorder and hypermobility-type Ehlers-Danlos syndrome: A narrative literature review *J Clin Med*. 2020;**9**:3992. https://doi.org/10.3390/jcm9123992.
5. Blajwajs L, Williams J, Timmons W., *et al.* Hypermobility prevalence, measurements, and outcomes in childhood, adolescence, and emerging adulthood: A systematic review *Rheumatol Int*. 2023;**43**:1423–44. https://doi.org/10.1007/s00296-023-05338-x.
6. Liu Y, Suvithayasiri S, Kim JS Comparative efficacy of clinical interventions for sacroiliac joint pain: Systematic review and network meta-analysis with preliminary Design of Treatment Algorithm *Neurospine*. 2023;**20**:997–1010. https://doi.org/10.14245/ns.2346586.293.
7. Polly DW, Swofford J, Whang PG., *et al.* Two-year outcomes from a randomized controlled trial of minimally invasive sacroiliac joint fusion vs *Non-Surgical Management for Sacroiliac Joint Dysfunction Int J Spine Surg*. 2016;**10**:28. https://doi.org/10.14444/3028.
8. Sturesson B, Kools D, Pflugmacher R., *et al.* Six-month outcomes from a randomized controlled trial of minimally invasive SI joint fusion with triangular titanium implants vs conservative management *Eur Spine J*. 2017;**26**:708–19. https://doi.org/10.1007/s00586-016-4599-9.
9. Dengler J, Kools D, Pflugmacher R., *et al.* Randomized trial of sacroiliac joint arthrodesis compared with conservative Management for Chronic low back pain attributed to the sacroiliac joint *J Bone Joint Surg Am*. 2019;**101**:400–11. https://doi.org/10.2106/JBJS.18.00022.
10. Giannoudis PV (ed) Practical procedures in elective orthopaedic surgery: Pelvis and lower extremity chapter 3;

pp 23–29; 2012. https://www.google.co.uk/books/edition/Practical_Procedures_in_Elective_Orthopa/ZW9OLjs0v3oC?hl=en&gbpv=1&printsec=frontcover.
11. Makridis KG, Ahmad MA, Kanakaris NK., *et al.* Reconstruction of iliac crest with bovine cancellous allograft after bone graft harvest for symphysis pubis arthrodesis *Int Orthop*. 2012;**36**:1701–7. https://doi.org/10.1007/s00264-012-1572-z.
12. Tampieri A, Sprio S, Ruffini A., *et al.* From wood to bone: Multi-step process to convert wood hierarchical structures into biomimetic hydroxyapatite scaffolds for bone tissue engineering *J Mater Chem*. 2009;**19**:4973–80. https://doi.org/10.1039/b900333a.
13. Ruffini A, Sprio S, Tampieri A Study of the hydrothermal transformation of wood-derived calcium carbonate into 3D hierarchically organized hydroxyapatite *Chem Eng J*. 2013;**217**:150–8. https://doi.org/10.1016/j.cej.2012.11.107.
14. Beighton P, Solomon L, Soskolne CL Articular mobility in an African population *Ann Rheum Dis*. 1973;**32**:413–8. https://doi.org/10.1136/ard.32.5.413.
15. Garras DN, Carothers JT, Olson SA Single-leg-stance (flamingo) radiographs to assess pelvic instability: How much motion is normal? *J Bone Joint Surg Am*. 2008;**90**:2114–8. 10.2106/JBJS.G.00277.
16. Rubinstein LV, Steinberg SM, Kummar S., *et al.* The statistics of phase 0 trials *Stat Med*. 2010;**29**:1072–6. https://doi.org/10.1002/sim.3840.
17. Hanley JA, Lippman-Hand A If nothing goes wrong, is everything all right? *JAMA (Russkoe izd)*. 1983;**249**:1743–5. https://doi.org/10.1001/jama.249.13.1743.
18. Younger E, Chapman M Morbidity at bone graft donor sites *J Orthop Trauma*. 1989;**3**:192–5. https://doi.org/10.1097/00005131-198909000-00002.
19. Quigley J, Revie M, Dawson J Estimating risk when zero events have been observed *BMJ Qual Saf*. 2013;**22**:1042–3. https://doi.org/10.1136/bmjqs-2013-002246.
20. Younger E, Chapman M Morbidity at bone graft donor sites *J Orthop Trauma*. 1989;**3**:192–5. https://doi.org/10.1097/00005131-198909000-00002.
21. Rudolf L Sacroiliac joint arthrodesis-MIS technique with titanium implants: Report of the first 50 patients and outcomes *Open Orthop J*. 2012;**6**:495–502. https://doi.org/10.2174/1874325001206010495.
22. Gaetani P, Miotti D, Risso A, Bettaglio R, Bongetta D, Custodi V, Silvani V Percutaneous arthrodesis of sacro-iliac joint: A pilot study *J Neurosurg Sci*. 2013;**57**:297–301.
23. Dindo D, Demartines N, Clavien PA Classification of surgical complications: A new proposal with evaluation in a cohort of 6336 patients and results of a survey *Ann Surg*. 2004;**240**:205–13. https://doi.org/10.1097/01.sla.0000133083.54934.ae.
24. Lane JM, Sandhu HS Current approach to experimental bone grafting *Orthop Clin North Am*. 1987;**18**:213–25. https://doi.org/10.1016/S0030-5898(20)30385-0.
25. Wolf JM, Cameron KL, Owens BD Impact of joint laxity and hypermobility on the musculoskeletal system *J Am Acad Orthop Surg*. 2011;**19**:463–71. https://doi.org/10.5435/00124635-201108000-00002.
26. Kibsgård TJ, Røise O, Stuge B Pelvic joint fusion in patients with severe pelvic girdle pain—A prospective single-subject research design study *BMC Musculoskelet Disord*. 2014;**15**:85. https://doi.org/10.1186/1471-2474-15-85.
27. Martin CT, Haase L, Lender PA., *et al.* Minimally invasive sacroiliac joint fusion: The current evidence *Int J Spine Surg*. 2020;**14**:20–9. 10.14444/6072.
28. Dale M, Evans J, Carter K., *et al.* iFuse implant system for treating chronic sacroiliac joint pain: A NICE medical technology guidance *Appl Health Econ Health Policy*. 2020;**18**:363–73. https://doi.org/10.1007/s40258-019-00539-7.
29. Chau AM, Xu LL, van der Rijt R., *et al.* Reconstruction versus no reconstruction of iliac crest defects following harvest for spinal fusion: A systematic review: A review *J Neurosurg Spine*. 2012;**16**:565–72. https://doi.org/10.3171/2012.3.SPINE11979.
30. Bapat MR, Chaudhary K, Garg H., *et al.* Reconstruction of large iliac crest defects after graft harvest using autogenous rib graft: A prospective controlled study *Spine (Phila Pa 1976)*. 2008 Nov 1;**33**:2570–5. https://doi.org/10.1097/BRS.0b013e318185287d.
31. Zhang J, Wei Y, Gong Y., *et al.* Reconstruction of iliac crest defect after autogenous harvest with bone cement and screws reduces donor site pain *BMC Musculoskelet Disord*. 2018;**19**:237. https://doi.org/10.1186/s12891-018-2167-7.
32. He X, Han Q, Zhang Y., *et al.* Effect of collagen-based scaffolds with hydroxyapatite on the repair of cartilage defects in the rabbit knee joint *J Orthop Surg Res*. 2024;**19**:818. https://doi.org/10.1186/s13018-024-05323-5.
33. Kashte SB, Kadam S, Maffulli N., *et al.* Osteoinductive potential of graphene and graphene oxide for bone tissue engineering: A comparative study *J Orthop Surg Res*. 2024;**19**:527. https://doi.org/10.1186/s13018-024-05028-9.
34. Migliorini F, Pintore A, Vecchio G., *et al.* Ligament advanced reinforcement system (LARS) synthetic graft for PCL reconstruction: Systematic review and meta-analysis *Br Med Bull*. 2022;**143**:57–68. https://doi.org/10.1093/bmb/ldac011.

British Medical Bulletin, 2025, 153, 1–10
https://doi.org/10.1093/bmb/ldae023
Invited Review