

# Advances in Clinical and Medical Research

Genesis-ACMR-7(4)-131

Volume 7 | Issue 4

Open Access

ISSN: 2583-2778

## Regenerating Lumbar Discopathy: A Case Report of a New Enhanced Orthobiological Treatment Option and a New Enhanced Bone Marrow Aspirate Technique (B.E.S.T.B.M.A. — Bringing Excellence and Safety Technique for Best Marrow Aspirate)

Márcio Hiroaki Kume<sup>1\*</sup>, Bianca Furlan<sup>2</sup>, Camila Gobatto Boaventura<sup>2</sup>, Mônica Andréa Probst<sup>2</sup>, Edson Peracchi<sup>2</sup> and Carmen Austrália Paredes Marcondes Ribas<sup>3</sup>

<sup>1</sup>Sugisawa Hospital, Department of Regenerative Medicine, Curitiba, Brazil

<sup>2</sup>CeUnina, Department of Biologic Science, Curitiba, Brazil

<sup>3</sup>Mackenzie University, Curitiba, Brazil

**\*Corresponding author:** Márcio Hiroaki Kume, 80250-190, Iguassu Avenue, 1236, Sugisawa Hospital, Department of Regenerative Medicine, Curitiba, Brazil

**Citation:** Kume MH, Furlan B, Boaventura CG, Probst MA, Peracchi E, et al. Regenerating Lumbar Discopathy: A Case Report of a New Enhanced Orthobiological Treatment Option and a New Enhanced Bone Marrow Aspirate Technique (B.E.S.T.B.M.A. — Bringing Excellence and Safety Technique for Best Marrow Aspirate). *Adv Clin Med Res.* 7(4):1-17.

**Copyright**© 2026 by Kume MH, et al. All rights reserved. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

**Received:** August 17, 2026 | **Published:** September 15, 2026

### Abstract

**Background:** Bone marrow aspirate (BMA) for orthobiologic use is conventionally harvested from the posterior superior iliac spine (PSIS) through a postero-anterior corridor. When the gluteal and posterior iliac skin is compromised — by prior surgery, radiation, infection, or subcutaneous implants — that corridor may be unavailable, and no widely described alternative exists for the office-based orthobiologic setting. Progenitor yield is further limited by the well-documented dilution of marrow with peripheral blood when large volumes are drawn from a single site.

**Case presentation:** A 46-year-old man presented with two years of chronic low back pain and radicular symptoms. Magnetic resonance imaging showed L4–L5 disc degeneration with posterior bulging. Conservative management had failed, and a course of orthobiologic treatment performed one year earlier at another centre — BMA plus platelet-rich plasma (PRP) alone, three monthly sessions — had produced only about two weeks of relief after each session. Three months before the index procedure the patient had received bilateral hormone pellet implants in the superior gluteal region, which compromised both

conventional BMA entry points. He declined all non-orthobiologic options.

**Intervention:** Marrow was harvested with a new technique, designated B.E.S.T.B.M.A. (Bringing Excellence and Safety Technique for Best Marrow Aspirate). A single trocar was introduced tangentially to the lateral iliac crest, parallel to the cortical bone, and advanced in a cranio-caudal direction along the crest, away from the implanted gluteal zones. Six sequential 10 mL aspirations were performed, with the needle withdrawn 10 mm between each, for a total of 60 mL. The aspirate was processed into bone marrow aspirate concentrate (BMAC; 580 g for 10 min, then 1400 g for 6 min). Sixty millilitres of venous blood yielded PRP (400 g for 9 min) and a second, more concentrated preparation designated PRP plus (300 g for 15 min, then 700 g for 10 min). Lipoaspirate was emulsified for 15 min and passed through a 0.15 mm filter to produce nanofat, and a mechanically obtained stromal vascular fraction (SVF/VSF) was prepared (800 g for 15 min, then 1000 g for 10 min). The six products — native BMA, BMAC, PRP, PRP plus, nanofat and SVF — were injected together into the paravertebral compartment at the symptomatic level; no intradiscal injection was performed.

**Outcomes:** At six months the visual analogue scale (VAS) score for pain fell from 7 to 3 and the Oswestry Disability Index (ODI) from 48% to 22%, both exceeding accepted thresholds for minimal clinically important change [2,3]. Magnetic resonance imaging showed reduced paravertebral inflammatory signal and improved disc parameters. At twelve months the patient reported no pain and had returned fully to physical activity, and the treating team described the imaging appearance as complete regeneration of the discopathy. No adverse events were recorded.

**Conclusions:** In this single patient, a lateral cranio-caudal fractionated harvest allowed marrow to be obtained when both conventional posterior entry points were unusable, and a combined paravertebral orthobiologic injection was followed by sustained clinical and radiological improvement. A case report cannot establish efficacy: the natural course of low back pain, regression to the mean and placebo effects cannot be excluded [4–6], six biologics were given simultaneously so no component can be credited individually, no cell counts were obtained to confirm the presumed yield advantage of the harvest, and the claim of complete disc regeneration requires independent blinded radiological confirmation. The technique and the combined protocol are presented as hypothesis-generating and require controlled evaluation.

## Keywords

Bone marrow aspirate; Bone marrow aspirate concentrate; Platelet-rich plasma; Stromal vascular fraction; Nanofat; Lumbar disc degeneration; Iliac crest harvest; Batson plexus; Orthobiologics; Case report.

## Introduction

Degenerative disc disease is among the most common structural correlates of chronic low back pain, and a substantial proportion of patients remain symptomatic after exercise therapy, analgesia and image-guided injections [7,8]. Interest in orthobiologic treatment of the degenerative lumbar segment has grown accordingly, and the published clinical experience now includes intradiscal bone marrow concentrate [9,10], intradiscal culture-expanded and non-expanded mesenchymal stromal cells [11–13], intradiscal PRP and PRP releasate [14–16], intradiscal stromal vascular fraction with PRP [17], cell-based nucleus pulposus and chondrocyte products [18–20], and epidural platelet lysate for radicular pain [21]. Systematic reviews of this literature consistently report an acceptable short-term safety profile alongside low-certainty evidence of benefit and marked heterogeneity of preparation and delivery [22–26].

Almost all of that experience shares two design features. The first is the route of delivery: the biologic is placed inside the disc. Intradiscal delivery targets the nucleus pulposus directly, but it requires annular puncture, which carries a small but real risk of discitis and epidural abscess [27–30], and the puncture itself has been implicated in accelerating degeneration of the treated segment. The second is the source of the cells: marrow is aspirated from the posterior superior iliac spine (PSIS) through a postero-anterior corridor, a route supported by comparative yield data [31,32], by computed tomography and magnetic resonance corridor analyses [33,34] and by an extensive haematology safety record [35,36].

Both assumptions can fail in ordinary practice. The posterior corridor becomes unattractive or unusable when the overlying gluteal and posterior iliac soft tissue is compromised — after surgery, radiation, local infection, extensive scarring, or the presence of subcutaneous implants. Subcutaneous hormone pellets are implanted in exactly this region in very large numbers [37–39], and although the reported complication rate is low, local granulomatous and inflammatory reactions do occur [40] and most operators would not aspirate marrow through, or immediately adjacent to, a recently implanted pellet bed. To our knowledge, no alternative harvest corridor has been described specifically for the office-based orthobiologic setting in this situation.

A second, independent limitation applies to every harvest. Progenitor concentration in a marrow aspirate falls steeply as the volume drawn from a single site increase, because the aspirate is progressively diluted with peripheral blood. This has been demonstrated repeatedly since the original aspiration-volume study of Muschler and colleagues [41–44] and it is the reason the small-volume, multiple-position, fractionated harvest is recommended in technique descriptions written for orthobiologic practice [45,46].

This report describes the management of a patient in whom both problems were present at once. Both conventional posterior entry points were occupied by recently implanted hormone pellets, and the patient had already failed a conventional BMA-plus-PRP protocol at another centre. A harvest technique was therefore devised that enters lateral to the crest, runs tangentially and cranio-caudally along the iliac wing, and is fractionated by design. The technique is designated B.E.S.T.B.M.A. — Bringing Excellence and Safety Technique for Best Marrow Aspirate — and each letter maps onto a specific operational requirement (**Figure 1, Table 2**). The harvested marrow was combined with five other autologous preparations and delivered paravertebrally rather than intradiscally.

The report has three aims: to describe the harvest technique in sufficient detail for it to be reproduced and criticised; to document the preparation parameters of all six biologic products (All In - One Step Procedure), since incomplete reporting is the principal weakness of the orthobiologic literature [47–49]; and to set out honestly what a single uncontrolled observation can and cannot support.

### The B.E.S.T.B.M.A. extraction technique

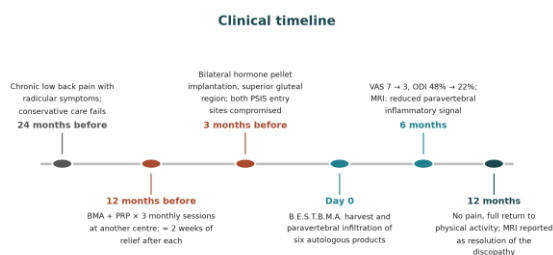
Bringing Excellence and Safety Technique for Best Marrow Aspirate

|          |                   |                                                                                                                         |
|----------|-------------------|-------------------------------------------------------------------------------------------------------------------------|
| <b>B</b> | <b>Bringing</b>   | One skin puncture brings the whole harvest through a single corridor giving access to six separate marrow beds          |
| <b>E</b> | <b>Excellence</b> | Every aspiration is limited to 10 mL, the range in which progenitor concentration is best preserved                     |
| <b>S</b> | <b>Safety</b>     | Entry lateral to the crest and tangential to the cortex, away from the sciatic notch, sacroiliac joint and implant beds |
| <b>T</b> | <b>Technique</b>  | The needle is advanced parallel to the cortex in a cranio-caudal direction along the iliac wing, not across it          |
| <b>B</b> | <b>Best</b>       | The needle is withdrawn 10 mm between draws, so each fraction comes from previously unaspirated cancellous bone         |
| <b>M</b> | <b>Marrow</b>     | Six fractions of 10 mL are pooled into 60 mL of anticoagulated aspirate                                                 |
| <b>A</b> | <b>Aspirate</b>   | The pooled aspirate is divided: one portion stays native, the remainder is concentrated                                 |

Each element is an operational specification, not a slogan; the corresponding parameters are listed in Table 2.

**Table 1:** Patient and baseline characteristics | Items marked as not recorded were not available in the source clinical record and must be completed before submission.

VAS, visual analogue scale; ODI, Oswestry Disability Index; BMA, bone marrow aspirate; PRP, platelet-rich plasma; PSIS, posterior superior iliac spine; SLR, straight leg raise; BMI, body mass index.



Timing as reported by the treating physician; the previous course was not documented with validated scores.

**Figure 2:** Clinical timeline | Sequence of events from symptom onset to the twelve-month assessment, including the failed conventional orthobiologic course and the gluteal pellet implantation that determined the choice of harvest corridor.

## The B.E.S.T.B.M.A. Harvest Technique

### Rationale and naming

The technique was designed to satisfy four constraints simultaneously: to avoid the compromised gluteal soft tissue bilaterally; to remain within cancellous bone along a long, predictable corridor; to keep every individual aspiration small so that peripheral blood dilution is minimised [41-43]; and to sample distinct marrow beds rather than repeatedly emptying one. The acronym B.E.S.T.B.M.A. — Bringing Excellence and Safety Technique for Best Marrow Aspirate — encodes these requirements as a teaching mnemonic (**Figure 1, Table 2**) gives the operational specification behind each letter. The mnemonic is a description of the technique, not a validated scoring instrument.

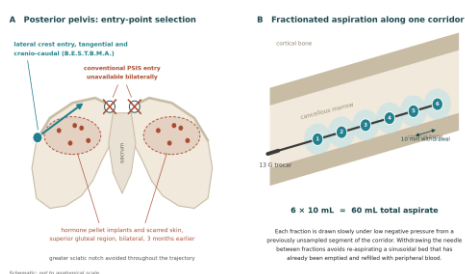
| Letter   | Term       | Operational specification in this technique                                                                                                                                   |
|----------|------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>B</b> | Bringing   | A single skin puncture provides access to six separate marrow beds, so the entire harvest is brought through one corridor                                                     |
| <b>E</b> | Excellence | Every aspiration is limited to 10 mL, the volume range at which progenitor concentration is best preserved [41,43]                                                            |
| <b>S</b> | Safety     | Entry is lateral to the crest and tangential to the cortex, keeping the trajectory away from the sciatic notch, the sacroiliac joint and the compromised gluteal implant beds |
| <b>T</b> | Technique  | The needle is advanced parallel to the cortical bone in a cranio-caudal direction along the iliac wing rather than postero-anteriorly through it                              |
| <b>B</b> | Best       | The needle is withdrawn 10 mm between consecutive aspirations, so each 10 mL sample is drawn from previously unaspirated cancellous bone                                      |

| Letter | Term     | Operational specification in this technique                                                                          |
|--------|----------|----------------------------------------------------------------------------------------------------------------------|
| M      | Marrow   | Six fractions of 10 mL are pooled into a total of 60 mL of anticoagulated aspirate                                   |
| A      | Aspirate | The pooled aspirate is divided: one portion is kept native for injection and the remainder is concentrated (Table 4) |

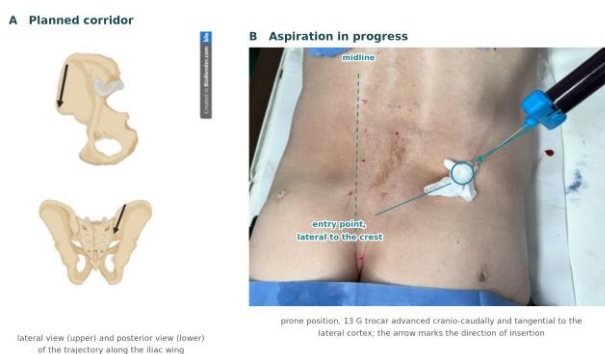
**Table 2:** Operational specification of the B.E.S.T.B.M.A. acronym | Each letter corresponds to a defined, reproducible step rather than to a descriptive quality.

### Positioning, entry point and trajectory

The patient was placed prone. The iliac crest was palpated and marked along its whole length; the posterior superior iliac spine and the bilateral gluteal pellet beds were marked separately as zones to be avoided. The skin entry point was chosen on the lateral aspect of the crest, well anterior and lateral to the pellet zone. After antisepsis and local anaesthesia of the skin, subcutaneous tissue and periosteum, a 13-gauge trocar was introduced tangentially to the lateral iliac crest so that the shaft lay parallel to the cortical bone rather than perpendicular to it, and was advanced in a cranio-caudal direction within the cancellous bone of the iliac wing (Figures 3 and 4). Advancing along, rather than across, the wing provides a long intraosseous corridor and keeps the tip between the two cortical tables throughout.



**Figure 3:** Entry-point selection and fractionated aspiration | (A) Posterior view of the pelvis. The conventional posterior superior iliac spine entry points are crossed out because both were occupied by hormone pellet implant beds; the lateral cranio-caudal corridor used instead is shown in teal. (B) The six sequential aspiration positions along that corridor, each of 10 mL, with the needle withdrawn 10 mm between consecutive draws. Schematic; not to anatomical scale.



**Figure 4:** The technique in practice | (A) Illustration of the lateral cranio-caudal trajectory in lateral hemipelvic and posterior pelvic views. (B) Intraoperative photograph of the harvest in the prone patient, showing the 13-gauge trocar and aspirating syringe entering lateral to the left iliac crest and directed obliquely along the wing. Reproduced with the patient's written consent. The illustration in panel A was created in BioRender and requires a publication licence before submission.

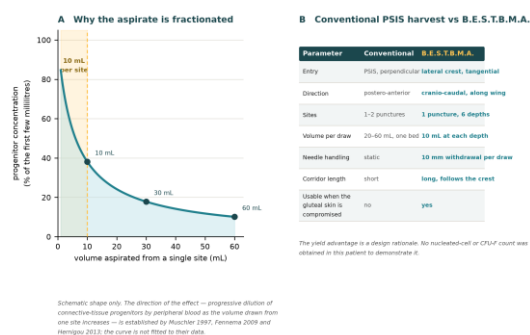
## Fractionated aspiration

Aspiration was performed with syringes pre-loaded with anticoagulant. Six sequential aspirations of 10 mL each were taken. Before each subsequent aspiration the needle was withdrawn by 10 mm along the same corridor, so that every fraction was drawn from a segment of cancellous bone that had not previously been aspirated. Aspiration was performed slowly with gentle, intermittent negative pressure. The six fractions were pooled to give 60 mL of anticoagulated bone marrow aspirate. The rationale for this fractionation, and the contrast with a conventional harvest, are shown in (Figure 5 and Table 3).

| Parameter                                     | Conventional PSIS harvest                    | B.E.S.T.B.M.A. (this case)        |
|-----------------------------------------------|----------------------------------------------|-----------------------------------|
| Patient position                              | Prone                                        | Prone                             |
| Entry point                                   | Posterior superior iliac spine               | Lateral aspect of the iliac crest |
| Needle orientation relative to cortex         | Perpendicular                                | Tangential (parallel to cortex)   |
| Direction of advancement                      | Postero-anterior, across the wing            | Cranio-caudal, along the wing     |
| Skin punctures                                | 1–2 (often bilateral)                        | 1                                 |
| Distinct marrow beds sampled                  | 1–2                                          | 6 (one per 10 mm withdrawal)      |
| Volume per aspiration                         | Frequently 20–60 mL from one bed             | 10 mL                             |
| Needle repositioning between draws            | Variable / none                              | 10 mm withdrawal before each draw |
| Total volume aspirated                        | Variable                                     | 60 mL                             |
| Needle gauge                                  | 11–13 G                                      | 13 G                              |
| Anticoagulation                               | Yes                                          | Yes                               |
| Guidance                                      | Landmark, fluoroscopic or ultrasound [33,34] | Landmark (palpation)              |
| Feasible with compromised gluteal soft tissue | No                                           | Yes                               |

**Table 3:** Conventional posterior harvest compared with the B.E.S.T.B.M.A. technique | The conventional column describes common practice as reported in the cited technique and imaging literature and is provided for orientation; it is not a comparator arm.

PSIS, posterior superior iliac spine. No nucleated cell counts or colony-forming unit–fibroblast assay was performed in this patient, so the presumed yield advantage of the fractionated corridor is a design rationale rather than a measured outcome.



**Figure 5:** Why the harvest is fractionated, and how it differs from the conventional route | (A) Schematic representation of the established inverse relationship between the volume drawn from a single site and the concentration of connective-tissue progenitors in the aspirate. (B) Parameter-by-parameter contrast between the conventional posterior harvest and the technique used here.

## Preparation of the Six Biologic Products – all in – One Step Procedure

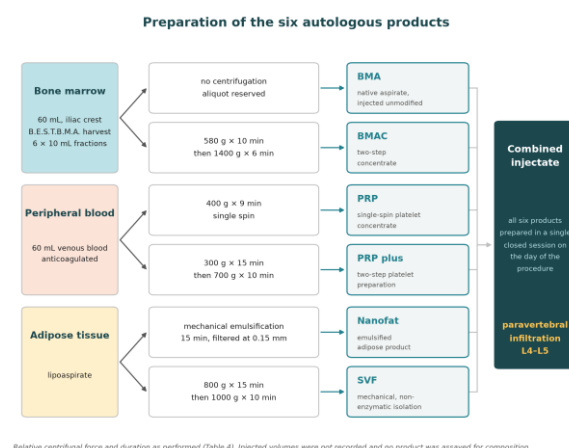
Six autologous preparations were used. All processing was performed on the day of the procedure, in a closed system, using centrifugation only; no enzymatic digestion, no culture expansion, no

cryopreservation and no addition of non-autologous substances were involved. Mechanical, non-enzymatic isolation was chosen for the adipose-derived products because it avoids collagenase digestion and its associated regulatory classification [50–52]. (Table 4) gives the full parameter set and (Figure 6) shows the workflow.

| Product           | Starting material                                    | Processing                                                                     | Use in this case                                    |
|-------------------|------------------------------------------------------|--------------------------------------------------------------------------------|-----------------------------------------------------|
| <b>Native BMA</b> | 60 mL anticoagulated marrow (B.E.S.T.B.M.A. harvest) | None beyond pooling; an aliquot reserved unprocessed                           | Injected unmodified                                 |
| <b>BMAC</b>       | Pooled marrow aspirate                               | 580 g for 10 min, then 1400 g for 6 min                                        | Concentrated nucleated cell and progenitor fraction |
| <b>PRP</b>        | 60 mL peripheral venous blood                        | 400 g for 9 min                                                                | Standard single-spin platelet concentrate           |
| <b>PRP plus</b>   | Peripheral venous blood                              | 300 g for 15 min, then 700 g for 10 min                                        | Second, more concentrated platelet preparation      |
| <b>Nanofat</b>    | Lipoaspirate                                         | Mechanical emulsification for 15 min, then filtration through a 0.15 mm filter | Emulsified adipose product                          |
| <b>SVF (VSF)</b>  | Lipoaspirate                                         | 800 g for 15 min, then 1000 g for 10 min                                       | Mechanically obtained stromal vascular fraction     |

**Table 4:** Preparation protocols for all six autologous products | Centrifugation is expressed as relative centrifugal force (g) and duration exactly as performed.

BMA, bone marrow aspirate; BMAC, bone marrow aspirate concentrate; PRP, platelet-rich plasma; SVF, stromal vascular fraction (VSF in the original record). No platelet, leucocyte, nucleated cell or viability count was obtained for any product. Consequently, none of the preparations can be placed within the PAW [53], DEPA [54] or MARSPIILL [55] classifications, and the report does not meet the composition-reporting standards recommended for orthobiologic studies [47–49]. Cells within the SVF and nanofat preparations were not characterised against the IFATS/ISCT [56] or ISCT [57] criteria and are therefore described by their method of preparation rather than by phenotype.



**Figure 6:** Preparation workflow | Three autologous starting materials — bone marrow, peripheral blood and lipoaspirate — were processed by centrifugation and mechanical emulsification into six products, which were combined into a single injectate. Relative centrifugal force and duration are shown for each step.

## Target Selection and Injection

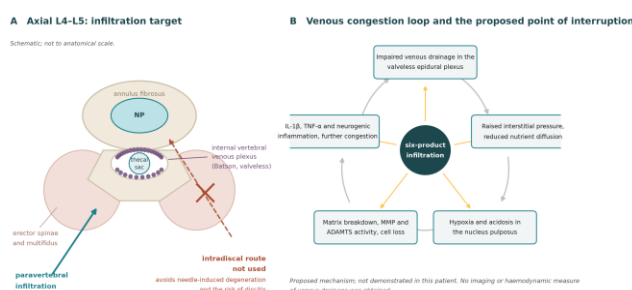
### Why paravertebral rather than intradiscal

The great majority of published disc-directed orthobiologic protocols inject into the nucleus pulposus [9,11,14,15,17,58]. Three considerations led to a paravertebral target in this patient. First, annular puncture is not without hazard: discitis and epidural abscess after intradiscal procedures are rare but well



documented [27–30], and the avascular disc is a poor environment in which to defend against inoculation. Second, needle puncture of the annulus is itself a recognised stimulus to further degeneration, which is difficult to justify in a segment that is already degenerate. Third, the paravertebral compartment contains the structures through which venous drainage of the segment occurs.

The vertebral venous system described by Batson is valveless and continuous with the paravertebral, epidural and pelvic venous networks [59–61]. Distension of this plexus has been proposed, and demonstrated venographically, as a contributor to lumbar radicular symptoms independent of mechanical compression [62,63]. If venous congestion contributes to the inflammatory and nociceptive state of the segment, then a biologic delivered into the paravertebral tissue acts on the compartment in which that congestion occurs, without breaching the annulus. This reasoning is mechanistic and hypothetical; it was not tested in this patient. (**Figure 7**) sets out the anatomical argument.



**Figure 7:** Anatomical rationale for the paravertebral target | (A) Axial schematic at L4–L5 showing the valveless paravertebral and epidural components of Batson's plexus, the paravertebral injection path used, and the intradiscal route that was deliberately avoided. (B) The proposed venous congestion loop and the points at which a paravertebral biologic is postulated to interrupt it. Panel B is a hypothesis, not a measured pathway.

| Item                              | Detail as performed                                                                            |
|-----------------------------------|------------------------------------------------------------------------------------------------|
| Target compartment                | Paravertebral soft tissue at the symptomatic level                                             |
| Level                             | L4–L5                                                                                          |
| Laterality                        | bilateral                                                                                      |
| Products injected                 | Native BMA + BMAC + PRP + PRP plus + nanofat + SVF, combined                                   |
| Volume per product / total volume | 20 ml                                                                                          |
| Needle gauge and length           | 20 G / 40mm                                                                                    |
| Image guidance                    | ultrasound                                                                                     |
| Intradiscal injection             | <b>Not performed</b>                                                                           |
| Number of sessions                | <b>One</b>                                                                                     |
| Post-procedure protocol           | activity restriction 7 days, analgesia with paracetamol 500mg 6/6h, rehabilitation immediately |

**Table 5:** Injection map | Fields marked for insertion were not documented in the source record and are required for the procedure to be reproducible.

BMA, bone marrow aspirate; BMAC, bone marrow aspirate concentrate; PRP, platelet-rich plasma; SVF, stromal vascular fraction.

## Outcomes and Follow-Up

Follow-up was clinical and radiological at six and twelve months. Pain was recorded on a 0–10 visual analogue scale and function with the Oswestry Disability Index [64,65].



At six months the VAS score had fallen from 7 to 3 and the ODI from 48% to 22%. Both changes exceed the commonly cited thresholds for minimal clinically important change in chronic low back pain — approximately 2 points or 30% for pain, and approximately 10 percentage points for the ODI [2,3,66]. Magnetic resonance imaging at six months showed reduced paravertebral inflammatory signal and improved disc parameters. At twelve months the patient reported no pain and had returned fully to physical activity; the treating team described the twelve-month imaging as showing complete regeneration of the discopathy. A twelve-month ODI was not recorded. No adverse event, infection, bleeding complication, neurological deficit or pellet-related problem occurred at either the harvest or the injection site during the twelve months of observation.

| Timepoint | VAS (0–10)           | Change from baseline | ODI (%)      | Change from baseline | Exceeds MCID? |
|-----------|----------------------|----------------------|--------------|----------------------|---------------|
| Baseline  | 7                    | —                    | 48           | —                    | —             |
| 6 months  | 3                    | –4 points (–57%)     | 22           | –26 points           | Yes, both     |
| 12 months | 0 (no pain reported) | –7 points (–100%)    | not recorded | not calculable       | Yes, VAS      |

**Table 6:** Clinical outcomes against minimal clinically important change | Percentage changes are calculated from the reported scores.

VAS, visual analogue scale; ODI, Oswestry Disability Index; MCID, minimal clinically important change. Thresholds applied:  $\approx$  2 points or 30% improvement for pain and  $\approx$  10 percentage points for the ODI [2,3,66]. The twelve-month VAS is derived from the recorded statement that the patient had no pain. The absence of a twelve-month ODI is a reporting gap.

| MRI parameter                         | Baseline                        | 6 months                 | 12 months                         |
|---------------------------------------|---------------------------------|--------------------------|-----------------------------------|
| Disc degeneration, L4–L5              | Present, with posterior bulging | Improved disc parameters | Reported as complete regeneration |
| Pfirsman grade [67,68]                | Grade IV                        | Grade III                | Grade I                           |
| Posterior bulge (mm)                  | 3                               | 1                        | none                              |
| Disc height (mm or index)             | 8                               | 9                        | 9                                 |
| Modic changes [69,70]                 | Type II                         | Type I                   | Type I                            |
| Paravertebral inflammatory signal     | Increased                       | <b>Reduced</b>           | None                              |
| Quantitative T2 / T1p mapping [71,72] | Not performed                   | Not performed            | Not performed                     |
| Independent blinded read              | No                              | No                       | No                                |

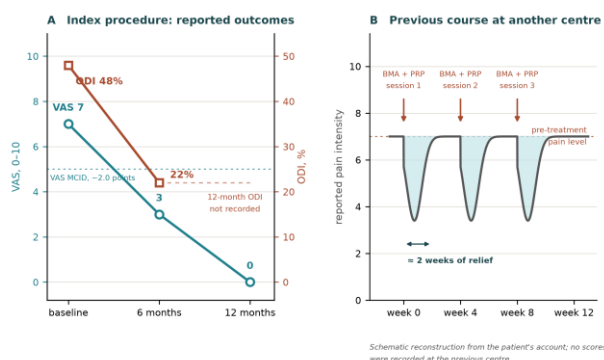
**Table 7:** Magnetic resonance findings by timepoint | Rows marked for insertion were not quantified in the source record. The narrative descriptions in bold are reproduced as recorded by the treating team.

The statement of complete regeneration is the treating team's interpretation of the twelve-month study. It is an extraordinary claim for a degenerate lumbar disc and cannot be accepted without the source images, graded Pfirsman scores at each timepoint and an independent blinded radiological read; quantitative T2 or T1p mapping would provide compositional rather than morphological evidence [71,72].

| Domain                                | Observation over 12 months                            |
|---------------------------------------|-------------------------------------------------------|
| Harvest site                          | No infection, haematoma, persistent pain or fracture  |
| Injection site                        | No infection, no neurological deficit, no bleeding    |
| Discitis                              | Not applicable — no annular puncture was performed    |
| Hormone pellet beds                   | No displacement, extrusion or local reaction reported |
| Systemic events                       | None reported                                         |
| Unanticipated events                  | None reported                                         |
| Adverse event grading instrument used | None                                                  |

**Table 8:** Safety and adverse events | Ascertainment was by clinical review at scheduled visits; no formal adverse-event instrument was applied.

For context, a multicentre analysis of 2,372 patients treated with autologous cell therapy for orthopaedic conditions reported a low rate of serious adverse events [73]. Single-case safety observations carry no inferential weight.



**Figure 8:** Clinical trajectory | (A) Visual analogue scale and Oswestry Disability Index from baseline to twelve months, with minimal clinically important change thresholds indicated; the twelve-month ODI was not recorded. (B) The patient's previous course of conventional bone marrow aspirate and platelet-rich plasma at another centre, showing approximately two weeks of relief after each of three-monthly sessions.

## Discussion

### Principal observations

Three things happened in this case. A marrow harvest was completed through a corridor that has not, to our knowledge, been described for office-based orthobiologic practice, in a patient in whom both conventional entry points were unusable. Six autologous preparations were delivered together into the paravertebral compartment rather than into the disc. And the patient improved, by margins exceeding the minimal clinically important change, and remained improved at twelve months after a single session — in contrast to the roughly two weeks of relief he had obtained from each of three previous conventional sessions.

### The harvest corridor

The posterior superior iliac spine is preferred for good reasons: it yields more and more proliferative marrow than the anterior crest or the proximal humerus [31,32], the corridor has been mapped in three dimensions [33,34], and its safety record is extensive [35,36]. The lateral cranio-caudal corridor used here trades that evidence base for accessibility. Its theoretical advantages are a long intraosseous path between two cortical tables, which permits several distinct sampling depths from one puncture, and a trajectory that runs away from the sacroiliac joint, the sciatic notch and the pelvic cavity. Its disadvantages are that the marrow content of the lateral iliac wing is likely to be lower than that of the posterior spine, that the corridor has not been characterised radiologically, and that no cadaveric safety study of it exists. This last point should be stated plainly: there is at present no published anatomical validation of this corridor.

### Fractionation and yield

The decision to draw six 10 mL fractions, withdrawing the needle 10 mm between each, follows directly from the aspiration-volume literature. Muschler and colleagues showed that the concentration of osteoblastic progenitors falls sharply as aspiration volume from a single site increase [41]; the same

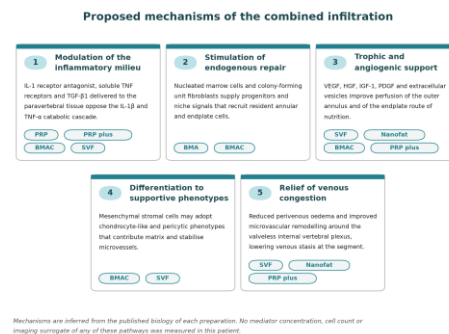
dilution effect has since been confirmed for mesenchymal stromal cells and for connective-tissue progenitors [42–44], and small-volume multi-site aspiration is now standard advice in orthobiologic technique descriptions [45,46]. The technique described here is a systematic implementation of that principle. Whether it actually delivered a higher progenitor dose in this patient is unknown, because no nucleated cell counts and no colony-forming unit–fibroblast assay were performed. Any future use of this technique should include those measurements; without them the central claim of the acronym remains unverified.

### Processing and the composition gap

Concentration systems differ substantially in the cell numbers they deliver from identical starting material [74–76], and mechanical adipose processing methods differ likewise in stromal cell recovery and viability [51,77–81]. Reporting the centrifugation parameters, as done in (Table 4), is necessary but not sufficient: without platelet, leucocyte and nucleated cell counts the products cannot be classified under PAW, DEPA or MARSPILL [53–55], and the report falls short of the MIBO and related reporting standards [47–49]. A recent international consensus statement identifies exactly this deficiency as a principal obstacle to interpreting orthobiologic outcomes [82].

### Proposed mechanisms

Five mechanisms can be proposed for the observed effect; all are plausible and none was measured (Figure 9). First, modulation of the local inflammatory cytokine environment by platelet-derived and marrow-derived mediators. Second, stimulation of endogenous repair within the annulus and adjacent tissue. Third, trophic and paracrine support of resident cells, which is now considered the dominant mode of action of non-expanded mesenchymal populations [7,26,83]. Fourth, differentiation of delivered stromal cells into supportive cell types, a mechanism demonstrated in animal disc models [84,85] but not confirmed in humans. Fifth, reduction of venous congestion within Batson's plexus, with consequent improvement in segmental drainage and reduction of the inflammatory load [59,61,62].



**Figure 9:** Proposed mechanisms | Five non-exclusive mechanisms by which the combined paravertebral injectate might act, with the products plausibly contributing to each. None of these pathways was measured in this patient; the figure summarises hypotheses.

| Study                      | Biologic                            | Route       | Design as published                             |
|----------------------------|-------------------------------------|-------------|-------------------------------------------------|
| Pettine 2015 / 2017 [9,10] | Bone marrow concentrates            | Intradiscal | Prospective cohort, 12-month and 3-year reports |
| Orozco 2011 [11]           | Autologous expanded bone marrow MSC | Intradiscal | Pilot study                                     |
| Noriega 2017 [12]          | Allogeneic bone marrow MSC          | Intradiscal | Randomised controlled trial                     |

| Study                    | Biologic                                           | Route                | Design as published                             |
|--------------------------|----------------------------------------------------|----------------------|-------------------------------------------------|
| Elabd 2016 [13]          | Autologous hypoxic cultured bone marrow MSC        | Intradiscal          | Long-term safety and feasibility, five patients |
| Kumar 2017 [58]          | Adipose-derived MSC with hyaluronic acid           | Intradiscal          | Phase I, one-year follow-up                     |
| Comella 2017 [17]        | Stromal vascular fraction with PRP                 | Intradiscal          | Prospective open-label study                    |
| Tuakli-Wosornu 2016 [14] | Platelet-rich plasma                               | Intradiscal          | Double-blind randomised controlled study        |
| Akeda 2017 [15]          | PRP releasate                                      | Intradiscal          | Preliminary clinical trial                      |
| Levi 2016 [16]           | Platelet-rich plasma                               | Intradiscal          | Prospective trial, preliminary results          |
| Centeno 2017 [21]        | Platelet lysate                                    | Lumbar epidural      | Registry-based series in radicular pain         |
| <b>Present report</b>    | <b>BMA + BMAC + PRP + PRP plus + nanofat + SVF</b> | <b>Paravertebral</b> | <b>Single case, uncontrolled</b>                |

**Table 9:** Position of this report within the published disc-directed orthobiologic literature | Only the biologic, route and published design are listed. Numerical outcomes are deliberately omitted because the preparations, populations, follow-up intervals and endpoints are not comparable, and a single case cannot be ranked against controlled studies.

MSC, mesenchymal stromal cells; PRP, platelet-rich plasma; BMA, bone marrow aspirate; BMAC, bone marrow aspirate concentrate; SVF, stromal vascular fraction. Systematic reviews of this field report low-certainty evidence and substantial heterogeneity [22-24,26].

### Regulatory context

All six preparations were autologous, prepared in a single operative session by centrifugation or mechanical emulsification, without enzymatic digestion or culture. In the United States this is the profile that determines whether a product falls under section 361 of the Public Health Service Act, through the minimal manipulation and homologous use criteria and the same surgical procedure exception [86,87]. In Brazil, advanced therapy products are governed by ANVISA resolutions RDC 505, 506 and 508 of 2021 [88]. Classification is jurisdiction-specific and depends on how the product is characterised and on the intended use; whether a paravertebral injection of adipose-derived material for disc degeneration is homologous use is not settled. Clinicians adopting this protocol must obtain their own regulatory determination. The wider concern that unproven autologous interventions are being offered ahead of evidence is well founded [89-91], and single-case reports such as this one should not be used in the promotion of a service.

### Limitations

- This is a single patient with no control and no blinding. No causal claim can be made.
- Chronic low back pain fluctuates, improves substantially under a wide range of treatments, and is strongly subject to regression to the mean; disc herniation and bulging also resorb spontaneously in a large proportion of cases [4–6,92,93]. Natural history and placebo effects cannot be excluded.
- Six biologic products were administered simultaneously. It is impossible to attribute the result to any one of them, to the combination, or to the new harvest technique.
- No nucleated cell count, colony-forming unit–fibroblast assay, platelet count, leucocyte count or viability assessment was performed for any product. The presumed yield advantage of the B.E.S.T.B.M.A. harvest is therefore an unverified design rationale, and the injectate cannot be characterised [47–49].

- The twelve-month claim of complete regeneration of the discopathy is not supported by graded, quantified or independently reviewed imaging. Pfirrmann grades, disc height and bulge measurements at each timepoint, the source images, and a blinded radiological read are all required before such a claim can stand [67,68].
- The twelve-month Oswestry Disability Index was not recorded, so the functional endpoint is incomplete.
- The lateral cranio-caudal corridor has not been validated in a cadaveric or imaging study, and its marrow content relative to the posterior superior iliac spine is unknown.
- The proposed contribution of venous congestion within Batson's plexus is a mechanistic hypothesis. No venographic, dynamic or quantitative imaging assessment of venous drainage was performed.
- Follow-up ended at twelve months. Durability beyond that point is unknown.
- Costs, access and regulatory classification differ between jurisdictions and may make the protocol unavailable to most patients.

## Conclusions

In a patient whose conventional posterior marrow harvest sites were both unusable because of recent gluteal hormone pellet implantation, a lateral cranio-caudal fractionated iliac harvest — designated B.E.S.T.B.M.A. — provided 60 mL of bone marrow aspirate through a single puncture, and a combined paravertebral injection of six autologous preparations was followed by clinically important and sustained improvement over twelve months, with no adverse events.

Two conclusions can reasonably be drawn. The harvest technique is feasible and offers a practical option when the posterior corridor is compromised. And a paravertebral target, which avoids annular puncture entirely, deserves formal comparison with the intradiscal route that dominates the current literature.

Neither the technique nor the protocol is validated by this report. What is needed next is a controlled study with cell-count characterisation of every product, blinded and quantified imaging endpoints including Pfirrmann grading and quantitative T2 mapping, a comparison of harvest corridors with progenitor yield as the primary endpoint, and a factorial or stepwise design capable of identifying which components of a combined injectate contribute to effect. Until such studies exist, the observations reported here should be treated as hypothesis-generating.

## Reporting Checklist

| CARE item                                    | Where addressed                          |
|----------------------------------------------|------------------------------------------|
| Title identifies the report as a case report | Title page                               |
| Key words                                    | End of abstract                          |
| Structured abstract                          | Abstract                                 |
| Introduction with background and rationale   | Section 1                                |
| Patient information and de-identification    | Section 2.1, Table 1                     |
| Clinical findings                            | Section 2.1, Table 1 (partly incomplete) |
| Timeline                                     | Figure 2                                 |
| Diagnostic assessment                        | Section 2.1, Table 7 (partly incomplete) |
| Therapeutic intervention, fully specified    | Sections 3–5, Tables 2–5, Figures 3–7    |
| Follow-up and outcomes                       | Section 6, Tables 6–8, Figure 8          |
| Adverse and unanticipated events             | Table 8                                  |
| Discussion with strengths and limitations    | Sections 7 and 8                         |
| Patient perspective                          | None                                     |
| Informed consent obtained                    | Yes                                      |

**Table 10:** Compliance with the CARE checklist for case reports [1] | Items marked for insertion must be completed before submission.

## Declarations

### Ethics approval and consent to participate

Institutional review board / research ethics committee approval. The patient provided written informed consent for the procedure.

### Consent for publication

Written informed consent for publication of the clinical details, the imaging and the intraoperative photograph reproduced in Figure 4B was obtained from the patient.

### Availability of data and materials

All data generated or analysed during this case are included in this article. The source magnetic resonance images are held by the treating institution and can be made available for independent review on reasonable request.

### Competing interests

The authors declare no competing interests.

### Funding

No funding was received.

### Authors' contributions

All authors read and approved the final manuscript.

### Acknowledgements

The illustration reproduced in (Figure 4A) was created in BioRender

### Use of artificial intelligence

Generative artificial intelligence tools were used in the preparation of the manuscript for analytic data and studies comparisons.

## References

1. Gagnier JJ, Kienle G, Altman DG, Moher D, Sox H, et al. (2013) The CARE guidelines: consensus-based clinical case reporting guideline development. *J Med Case Rep.* 7:223.
2. Ostelo RW, Deyo RA, Stratford P, Waddell G, Croft P, et al. (2008) Interpreting change scores for pain and functional status in low back pain: towards international consensus regarding minimal important change. *Spine (Phila Pa 1976).* 33(1):90-4.
3. Copay AG, Glassman SD, Subach BR, Berven S, Schuler TC, et al. (2008) Minimum clinically important difference in lumbar spine surgery patients: a choice of methods using the Oswestry Disability Index, Medical Outcomes Study questionnaire Short Form 36, and pain scales. *Spine J.* 8(6):968-74.
4. Whitney CW, Von Korff M. (1992) Regression to the mean in treated versus untreated chronic pain. *Pain.* 50(3):281-5.
5. Artus M, van der Windt DA, Jordan KP, Hay EM. (2010) Low back pain symptoms show a similar pattern of improvement following a wide range of primary care treatments: a systematic review of randomized clinical trials. *Rheumatology (Oxford).* 49(12):2346-56.
6. Artus M, van der Windt D, Jordan KP, Croft PR. (2014) The clinical course of low back pain: a meta-analysis comparing outcomes in randomised clinical trials and observational studies. *BMC Musculoskelet Disord.* 15:68.
7. Sakai D, Andersson GB. (2015) Stem cell therapy for intervertebral disc regeneration: obstacles and solutions. *Nat Rev Rheumatol.* 11(4):243-56.
8. Urits I, Viswanath O, Galasso AC, Sottosani ER, Mahan KM, et al. (2019) Platelet-rich plasma for the treatment of low back pain: a comprehensive review. *Curr Pain Headache Rep.* 23(7):52.

9. Pettine KA, Murphy MB, Suzuki RK, Sand TT. (2015) Percutaneous injection of autologous bone marrow concentrate cells significantly reduces lumbar discogenic pain through 12 months. *Stem Cells*. 33(1):146-56.
10. Pettine KA, Suzuki RK, Sand TT, Murphy MB. (2017) Autologous bone marrow concentrate intradiscal injection for the treatment of degenerative disc disease with three-year follow-up. *Int Orthop*. 41(10):2097-103.
11. Orozco L, Soler R, Morera C, Alberca M, Sánchez A, et al. (2011) Intervertebral disc repair by autologous mesenchymal bone marrow cells: a pilot study. *Transplantation*. 92(7):822-8.
12. Noriega DC, Ardura F, Hernández-Ramajo R, Martín-Ferrero MÁ, Sánchez-Lite I, et al. (2017) Intervertebral disc repair by allogeneic mesenchymal bone marrow cells: a randomized controlled trial. *Transplantation*. 101(8):1945-51.
13. Elabd C, Centeno CJ, Schultz JR, Lutz G, Ichim T, et al. (2016) Intra-discal injection of autologous, hypoxic cultured bone marrow-derived mesenchymal stem cells in five patients with chronic lower back pain: a long-term safety and feasibility study. *J Transl Med*. 14(1):253.
14. Tuakli-Wosornu YA, Terry A, Boachie-Adjei K, Harrison JR, Gribbin CK, et al. (2016) Lumbar intradiscal platelet-rich plasma (PRP) injections: a prospective, double-blind, randomized controlled study. *PM R*. 8(1):1-10.
15. Akeda K, Ohishi K, Masuda K, Bae WC, Takegami N, et al. (2017) Intradiscal injection of autologous platelet-rich plasma releasate to treat discogenic low back pain: a preliminary clinical trial. *Asian Spine J*. 11(3):380-9.
16. Levi D, Horn S, Tyszkowski S, Levin J, Hecht-Leavitt C, Walko E. (2016) Intradiscal platelet-rich plasma injection for chronic discogenic low back pain: preliminary results from a prospective trial. *Pain Med*. 17(6):1010-22.
17. Comella K, Silbert R, Parlo M. (2017) Effects of the intradiscal implantation of stromal vascular fraction plus platelet rich plasma in patients with degenerative disc disease. *J Transl Med*. 15(1):12.
18. Mochida J, Sakai D, Nakamura Y, Watanabe T, Yamamoto Y, et al. (2015) Intervertebral disc repair with activated nucleus pulposus cell transplantation: a three-year, prospective clinical study of its safety. *Eur Cell Mater*. 29:202-12.
19. Coric D, Pettine K, Sumich A, Boltes MO. (2013) Prospective study of disc repair with allogeneic chondrocytes: presented at the 2012 Joint Spine Section Meeting. *J Neurosurg Spine*. 18(1):85-95.
20. Meisel HJ, Siodla V, Ganey T, Minkus Y, Hutton WC, et al. (2007) Clinical experience in cell-based therapeutics: disc chondrocyte transplantation: a treatment for degenerated or damaged intervertebral disc. *Biomol Eng*. 24(1):5-21.
21. Centeno C, Markle J, Dodson E, Stemper I, Hyzy M, et al. (2017) The use of lumbar epidural injection of platelet lysate for treatment of radicular pain. *J Exp Orthop*. 4(1):38.
22. Meisel HJ, Agarwal N, Hsieh PC, Skelly A, Park JB, et al. (2019) Cell therapy for treatment of intervertebral disc degeneration: a systematic review. *Global Spine J*. 9(1):39-52.
23. Oehme D, Goldschlager T, Ghosh P, Rosenfeld JV, Jenkin G. (2015) Cell-based therapies used to treat lumbar degenerative disc disease: a systematic review of animal studies and human clinical trials. *Stem Cells Int*. 2015:946031.
24. Yim RL, Lee JT, Bow CH, Meij B, Leung V, et al. (2014) A systematic review of the safety and efficacy of mesenchymal stem cells for disc degeneration: insights and future directions for regenerative therapeutics. *Stem Cells Dev*. 23(21):2553-67.
25. Zeckser J, Wolff M, Tucker J, Goodwin J. (2016) Multipotent mesenchymal stem cell treatment for discogenic low back pain and disc degeneration. *Stem Cells Int*. 2016:3908389.
26. Sakai D, Schol J. (2017) Cell therapy for intervertebral disc repair: clinical perspective. *J Orthop Translat*. 9:8-18.
27. Subach BR, Copay AG, Martin MM, Schuler TC, DeWolfe DS. (2012) Epidural abscess and cauda equina syndrome after percutaneous intradiscal therapy in degenerative lumbar disc disease. *Spine J*. 12(11):e1-4.
28. Falagas ME, Bliziotis IA, Mavrogenis AF, Papagelopoulos PJ. (2006) Spondylodiscitis after facet joint steroid injection: a case report and review of the literature. *Scand J Infect Dis*. 38(4):295-9.
29. Bo W, Longyi C, Jian T, Guangfu H, Hailong F, et al. (2009) A pyogenic discitis at C3–C4 with associated ventral epidural abscess involving C1–C4 after intradiscal oxygen–ozone chemonucleolysis: a case report. *Spine (Phila Pa 1976)*. 34(8):E298-304.
30. Wu B, He X, Peng BG. (2020) Pyogenic discitis with an epidural abscess after cervical analgesic discography: a case report. *World J Clin Cases*. 8(11):2318-24.
31. Pierini M, Di Bella C, Dozza B, Frisoni T, Martella E, et al. (2013) The posterior iliac crest outperforms the anterior iliac crest when obtaining mesenchymal stem cells from bone marrow. *J Bone Joint Surg Am*. 95(12):1101-7.
32. Anz A, Sherman B. (2022) Concentrated bone marrow aspirate is more cellular and proliferative when harvested from the posterior superior iliac spine than the proximal humerus. *Arthroscopy*. 38(4):1110-4.
33. D'Souza RS, Li L, Leng S, Law L, et al. (2021) A three-dimensional computed tomography study to determine the ideal method for fluoroscopically-guided bone marrow aspiration from the iliac crest. *Bosn J Basic Med Sci*. 21(3):370-7.
34. Hirahara AM, Panero A, Andersen WJ. (2018) An MRI analysis of the pelvis to determine the ideal method for ultrasound-guided bone marrow aspiration from the iliac crest. *Am J Orthop (Belle Mead NJ)*. 47(5).
35. Bain BJ. (2003) Bone marrow biopsy morbidity and mortality. *Br J Haematol*. 121(6):949-51.
36. Long JR, Stensby JD, Wiesner EL, Bryson WN, Hillen TJ, et al. (2020) Efficacy and safety of bone marrow aspiration and biopsy using fluoroscopic guidance and a drill-powered needle: clinical experience from 775 cases. *Eur Radiol*. 30(11):5964-70.
37. Donovitz GS. (2021) Low complication rates of testosterone and estradiol implants for androgen and estrogen replacement therapy in over 1 million procedures. *Ther Adv Endocrinol Metab*. 12:20420188211015238.
38. Cavender RK, Fairall M. (2009) Subcutaneous testosterone pellet implant (Testopel) therapy for men with testosterone deficiency syndrome: a single-site retrospective safety analysis. *J Sex Med*. 6(11):3177-92.
39. Connors W, Flinn K, Morgentaler A. (2011) Outcomes with the "V" implantation technique vs. standard technique for testosterone pellet therapy. *J Sex Med*. 8(12):3465-70.
40. Patel MH, Brumfiel CM, Breen I, Glembocki D, Lubner A. (2023) Granulomatous panniculitis as a complication of subcutaneous testosterone pellet therapy. *Skinmed*. 21(3):203-4.
41. Muschler GF, Boehm C, Easley K. (1997) Aspiration to obtain osteoblast progenitor cells from human bone marrow: the influence of aspiration volume. *J Bone Joint Surg Am*. 79(11):1699-709.
42. Fennema EM, Renard AJ, Leusink A, van Blitterswijk CA, de Boer J. (2009) The effect of bone marrow aspiration strategy on the yield and quality of human mesenchymal stem cells. *Acta Orthop*. 80(5):618-21.



43. Hernigou P, Homma Y, Flouzat Lachaniette CH, Poignard A, Allain J, et al. (2013) Benefits of small volume and small syringe for bone marrow aspirations of mesenchymal stem cells. *Int Orthop*. 37(11):2279-87.
44. Patterson TE, Boehm C, Nakamoto C, Rozic R, Walker E, et al. (2017) The efficiency of bone marrow aspiration for the harvest of connective tissue progenitors from the human iliac crest. *J Bone Joint Surg Am*. 99(19):1673-82.
45. Chahla J, Mannava S, Cinque ME, Geeslin AG, Codina D, LaPrade RF. (2017) Bone marrow aspirate concentrate harvesting and processing technique. *Arthrosc Tech*. 6(2):e441-5.
46. Friedlis MF, Centeno CJ. (2016) Performing a better bone marrow aspiration. *Phys Med Rehabil Clin N Am*. 27(4):919-39.
47. Chahla J, Cinque ME, Piuze NS, Mannava S, Geeslin AG, et al. (2017) A call for standardization in platelet-rich plasma preparation protocols and composition reporting: a systematic review of the clinical orthopaedic literature. *J Bone Joint Surg Am*. 99(20):1769-79.
48. Murray IR, Geeslin AG, Goudie EB, Petrigliano FA, LaPrade RF. (2017) Minimum Information for Studies Evaluating Biologics in Orthopaedics (MIBO): platelet-rich plasma and mesenchymal stem cells. *J Bone Joint Surg Am*. 99(10):809-19.
49. Robinson PG, Murray IR, West CC, Goudie EB, Yong LY, et al. (2019) Reporting of mesenchymal stem cell preparation protocols and composition: a systematic review of the clinical orthopaedic literature. *Am J Sports Med*. 47(4):991-1000.
50. Aronowitz JA, Lockhart RA, Hakakian CS. (2015) Mechanical versus enzymatic isolation of stromal vascular fraction cells from adipose tissue. *Springerplus*. 4:713.
51. van Dongen JA, Tuin AJ, Spiekman M, Jansma J, van der Lei B, et al. (2018) Comparison of intraoperative procedures for isolation of clinical grade stromal vascular fraction for regenerative purposes: a systematic review. *J Tissue Eng Regen Med*. 12(1):e261-74.
52. Trivisonno A, Alexander RW, Baldari S, Cohen SR, Di Rocco G, et al. (2019) Intraoperative strategies for minimal manipulation of autologous adipose tissue for cell- and tissue-based therapies: concise review. *Stem Cells Transl Med*. 8(12):1265-71.
53. DeLong JM, Russell RP, Mazzocca AD. (2012) Platelet-rich plasma: the PAW classification system. *Arthroscopy*. 28(7):998-1009.
54. Magalon J, Chateau AL, Bertrand B, Louis ML, Silvestre A, et al. (2016) DEPA classification: a proposal for standardising PRP use and a retrospective application of available devices. *BMJ Open Sport Exerc Med*. 2(1):e000060.
55. Lana JFSD, Purita J, Paulus C, Huber SC, Rodrigues BL, et al. (2017) Contributions for classification of platelet rich plasma: proposal of a new classification: MARSPILL. *Regen Med*. 12(5):565-74.
56. Bourin P, Bunnell BA, Casteilla L, Dominici M, Katz AJ, et al. (2013) Stromal cells from the adipose tissue-derived stromal vascular fraction and culture expanded adipose tissue-derived stromal/stem cells: a joint statement of IFATS and ISCT. *Cytotherapy*. 15(6):641-8.
57. Dominici M, Le Blanc K, Mueller I, Slaper-Cortenbach I, Marini F, et al. (2006) Minimal criteria for defining multipotent mesenchymal stromal cells. The International Society for Cellular Therapy position statement. *Cytotherapy*. 8(4):315-7.
58. Kumar H, Ha DH, Lee EJ, Park JH, Shim JH, et al. (2017) Safety and tolerability of intradiscal implantation of combined autologous adipose-derived mesenchymal stem cells and hyaluronic acid in patients with chronic discogenic low back pain: 1-year follow-up of a phase I study. *Stem Cell Res Ther*. 8(1):262.
59. Batson OV. (1940) The function of the vertebral veins and their role in the spread of metastases. *Ann Surg*. 112(1):138-49.
60. Nathoo N, Caris EC, Wiener JA, Mendel E. (2011) History of the vertebral venous plexus and the significant contributions of Breschet and Batson. *Neurosurgery*. 69(5):1007-14.
61. Groen RJM, du Toit DF, Phillips FM, Hoogland PV, Kuizenga K et al. (2004) Anatomical and pathological considerations in percutaneous vertebroplasty and kyphoplasty: a reappraisal of the vertebral venous system. *Spine (Phila Pa 1976)*. 29(13):1465-71.
62. LaBan MM, Wilkins JC, Wesolowski DP, Bergeon B, Szappanos BJ. (2001) Paravertebral venous plexus distention (Batson's): an inciting etiologic agent in lumbar radiculopathy as observed by venous angiography. *Am J Phys Med Rehabil*. 80(2):129-33.
63. LaBan MM, McNeary L. (2008) The clinical value of B-type natriuretic peptide in predicting nocturnal low back pain in patients with concurrent lumbar spinal stenosis and cardiopulmonary dysfunction (Vesper's Curse): a clinical case series. *Am J Phys Med Rehabil*. 87(10):798-802.
64. Fairbank JC, Pynsent PB. (2000) The Oswestry Disability Index. *Spine (Phila Pa 1976)*. 25(22):2940-52.
65. Fairbank JC. (2014) Why are there different versions of the Oswestry Disability Index? *J Neurosurg Spine*. 20(1):83-6.
66. van der Roer N, Ostelo RW, Bekkering GE, van Tulder MW, de Vet HC. (2006) Minimal clinically important change for pain intensity, functional status, and general health status in patients with nonspecific low back pain. *Spine (Phila Pa 1976)*. 31(5):578-82.
67. Pfirrmann CW, Metzdorf A, Zanetti M, Hodler J, Boos N. (2001) Magnetic resonance classification of lumbar intervertebral disc degeneration. *Spine (Phila Pa 1976)*. 26(17):1873-8.
68. Urrutia J, Besa P, Campos M, Cikutovic P, Cabezon M, et al. (2016) The Pfirrmann classification of lumbar intervertebral disc degeneration: an independent inter- and intra-observer agreement assessment. *Eur Spine J*. 25(9):2728-33.
69. Modic MT, Steinberg PM, Ross JS, Masaryk TJ, Carter JR. (1988) Degenerative disk disease: assessment of changes in vertebral body marrow with MR imaging. *Radiology*. 166(1 Pt 1):193-9.
70. Hopayian K, Raslan E, Soliman S. (2023) The association of Modic changes and chronic low back pain: a systematic review. *J Orthop*. 35:99-106.
71. Marinelli NL, Haughton VM, Muñoz A, Anderson PA. (2009) T2 relaxation times of intervertebral disc tissue correlated with water content and proteoglycan content. *Spine (Phila Pa 1976)*. 34(5):520-4.
72. Yang L, Sun C, Gong T, Li Q, Chen X, et al. (2022) T1p, T2 and T2\* mapping of lumbar intervertebral disc degeneration: a comparison study. *BMC Musculoskelet Disord*. 23(1):1135.
73. Centeno CJ, Al-Sayegh H, Freeman MD, Smith J, Murrell WD, et al. (2016) A multi-center analysis of adverse events among two thousand, three hundred and seventy-two adult patients undergoing adult autologous stem cell therapy for orthopaedic conditions. *Int Orthop*. 40(8):1755-65.
74. Hegde V, Shonuga O, Ellis S, Fragomen A, Kennedy J, et al. (2014) A prospective comparison of 3 approved systems for autologous bone marrow concentration demonstrated nonequivalency in progenitor cell number and concentration. *J Orthop Trauma*. 28(10):591-8.
75. Dragoo JL, Guzman RA. (2020) Evaluation of the consistency and composition of commercially available bone marrow aspirate concentrate systems. *Orthop J Sports Med*. 8(1):2325967119893634.

76. Schäfer R, DeBaun MR, Fleck E, Centeno CJ, Kraft D, et al. (2019) Quantitation of progenitor cell populations and growth factors after bone marrow aspirate concentration. *J Transl Med.* 17(1):115.
77. Tonnard P, Verpaele A, Peeters G, Hamdi M, Cornelissen M, et al. (2013) Nanofat grafting: basic research and clinical applications. *Plast Reconstr Surg.* 132(4):1017-26.
78. Osinga R, Menzi NR, Tchang LAH, Caviezel D, Kalbermatten DF, et al. (2015) Effects of intersyringe processing on adipose tissue and its cellular components: implications in autologous fat grafting. *Plast Reconstr Surg.* 135(6):1618-28.
79. Chen X, Hong S, Hong F, Yang B, Tong C, Zhang J. (2020) Mechanical emulsification of lipoaspirate by different Luer-Lok connector changes the viability of adipose derived stem cells in nanofat. *J Plast Surg Hand Surg.* 54(6):344-51.
80. Cohen SR, Tiryaki T, Womack HA, Canikyan S, Schlaudraff KU, Schefflan M. (2019) Cellular optimization of nanofat: comparison of two nanofat processing devices in terms of cell count and viability. *Aesthet Surg J Open Forum.* 1(4):ojz028.
81. Schipper JAM, van Laarhoven CJHCM, Schepers RH, Tuin AJ, Harmsen MC, et al. (2023) Mechanical fractionation of adipose tissue: a scoping review of procedures to obtain stromal vascular fraction. *Bioengineering (Basel).* 10(10):1175.
82. Kunze KN, Morgan JT, Gerhold C, Nishioka T, Piuze NS, et al. (2026) An international expert consensus statement defining the best practices and areas of uncertainty concerning the use of orthobiologics. *J Bone Joint Surg Am.*
83. Vadalà G, Russo F, Ambrosio L, Papalia R, Denaro V. (2016) Mesenchymal stem cells for intervertebral disc regeneration. *J Biol Regul Homeost Agents.* 30(4 Suppl 1):173-9.
84. Acosta FL Jr, Metz L, Adkisson HD, Liu J, Carruthers-Liebenberg E, et al. (2011) Porcine intervertebral disc repair using allogeneic juvenile articular chondrocytes or mesenchymal stem cells. *Tissue Eng Part A.* 17(23–24):3045-55.
85. Wang Z, Perez-Terzic CM, Smith J, Mauck WD, Shelerud RA, et al. (2015) Efficacy of intervertebral disc regeneration with stem cells: a systematic review and meta-analysis of animal-controlled trials. *Gene.* 564(1):1-8.
86. US Food and Drug Administration. Regulatory considerations for human cells, tissues, and cellular and tissue-based products: minimal manipulation and homologous use — guidance for industry and Food and Drug Administration staff. Silver Spring: FDA.
87. US Food and Drug Administration, Center for Biologics Evaluation and Research. Same surgical procedure exception under 21 CFR 1271.15(b): questions and answers regarding the scope of the exception — guidance for industry. Silver Spring: FDA.
88. Agência Nacional de Vigilância Sanitária (ANVISA). Resoluções da Diretoria Colegiada RDC nº 505/2021, RDC nº 506/2021 and RDC nº 508/2021 on advanced therapy products, investigational advanced therapy products and good practice in human cells for therapeutic use. Brasília: ANVISA; 2021.
89. Marks P, Gottlieb S. (2018) Balancing safety and innovation for cell-based regenerative medicine. *N Engl J Med.* 378(10):954-9.
90. Marks PW, Hahn S. (2020) Identifying the risks of unproven regenerative medicine therapies. *JAMA.* 324(3):241-2.
91. Turner L. (2018) The US direct-to-consumer marketplace for autologous stem cell interventions. *Perspect Biol Med.* 61(1):7-24.
92. Chiu CC, Chuang TY, Chang KH, Wu CH, Lin PW, et al. (2015) The probability of spontaneous regression of lumbar herniated disc: a systematic review. *Clin Rehabil.* 29(2):184-95.
93. Zhong M, Liu JT, Jiang H, Mo W, Yu PF, et al. (2017) Incidence of spontaneous resorption of lumbar disc herniation: a meta-analysis. *Pain Physician.* 20(1):E45-52.