



UWL REPOSITORY

repository.uwl.ac.uk

How are adjacent spinal levels affected by vertebral fracture and by vertebroplasty? A biomechanical study on cadaveric spines

Luo, Jin ORCID logoORCID: <https://orcid.org/0000-0001-5451-9535>, Annesley-Williams, DJ, Adams, MA and Dolan, P (2017) How are adjacent spinal levels affected by vertebral fracture and by vertebroplasty? A biomechanical study on cadaveric spines. *The Spine Journal*, 17 (6). pp. 863-874. ISSN 1529-9430

<http://dx.doi.org/10.1016/j.spinee.2017.01.013>

This is the Accepted Version of the final output.

UWL repository link: <https://repository.uwl.ac.uk/id/eprint/6899/>

Alternative formats: If you require this document in an alternative format, please contact: open.research@uwl.ac.uk

Copyright: Creative Commons: Attribution-Noncommercial-No Derivative Works 4.0

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy: If you believe that this document breaches copyright, please contact us at open.research@uwl.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.

Rights Retention Statement:

Accepted Manuscript

Title: How are adjacent spinal levels affected by vertebral fracture, and by vertebroplasty? a biomechanical study on cadaveric spines

Author: Jin Luo, Deborah J. Annesley-Williams, Michael A. Adams, Patricia Dolan

PII: S1529-9430(17)30038-4
DOI: <http://dx.doi.org/doi: 10.1016/j.spinee.2017.01.013>
Reference: SPINEE 57242

To appear in: *The Spine Journal*

Received date: 15-8-2016
Revised date: 21-12-2016
Accepted date: 30-1-2017



Please cite this article as: Jin Luo, Deborah J. Annesley-Williams, Michael A. Adams, Patricia Dolan, How are adjacent spinal levels affected by vertebral fracture, and by vertebroplasty? a biomechanical study on cadaveric spines, *The Spine Journal* (2017), <http://dx.doi.org/doi: 10.1016/j.spinee.2017.01.013>.

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23

How are adjacent spinal levels affected by vertebral fracture, and by vertebroplasty?

A biomechanical study on cadaveric spines.

Jin Luo PhD*, Deborah J. Annesley-Williams FRCR[†],

Michael A. Adams PhD, Patricia Dolan PhD

Centre for Comparative and Clinical Anatomy, University of Bristol, Bristol, U.K.

* Department of Life Sciences, London South Bank University, London, U.K.

[†]Department of Neuroradiology, Queen's Medical Centre, Nottingham, U.K.

Corresponding author:

Dr Patricia Dolan

Centre for Comparative and Clinical Anatomy,

University of Bristol, Sowerth Street, Bristol BS2 8EJ, U.K.

Tel: +44 (0) 117 9288363

E-mail: Trish.Dolan@bris.ac.uk

1 **Abstract**

2 **Background Context:** Spinal injuries and surgery may have important effects at
3 neighbouring spinal levels, but previous investigations of adjacent-level biomechanics have
4 produced conflicting results. We use ‘stress profilometry’ and non-contact strain
5 measurements to investigate thoroughly this long-standing problem.

6 **Purpose:** To determine how vertebral fracture and vertebroplasty affect compressive load-
7 sharing and vertebral deformations at adjacent spinal levels.

8 **Study Design:** Mechanical experiments on cadaver spines.

9 **Methods:** 28 cadaveric spine specimens, comprising three thoracolumbar vertebrae and the
10 intervening discs and ligaments, were dissected from 14 spines aged 67-92 yrs. A needle-
11 mounted pressure transducer was used to measure the distribution of compressive stress
12 across the antero-posterior diameter of both intervertebral discs. ‘Stress profiles’ were
13 analysed to quantify intradiscal pressure (IDP), and concentrations of compressive stress in
14 the anterior and posterior annulus. Summation of stresses over discrete areas yielded the
15 compressive force acting on the anterior and posterior halves of each vertebral body, and the
16 compressive force resisted by the neural arch. Creep deformations of fractured and adjacent
17 vertebral bodies *under load* were measured using an optical MacReflex system. All
18 measurements were repeated following compressive injury to one of the three vertebrae, and
19 again after the injury had been treated by vertebroplasty. The study was funded by a grant
20 from Action Medical Research, UK (\$143,230). Authors of this study have no conflicts of
21 interest to disclose.

22 **Results:** Injury usually involved endplate fracture, often combined with deformation of the
23 anterior cortex, so that the affected vertebral body developed slight anterior wedging. Injury
24 reduced IDP at the affected level, to an average 47% of pre-fracture values ($P < 0.001$), and

1 transferred compressive load-bearing from nucleus to annulus, and also from disc to neural
2 arch. Similar but reduced effects were seen at adjacent (non-fractured) levels, where mean
3 IDP was reduced to 73% of baseline values ($P<0.001$). Vertebroplasty partially reversed these
4 changes, increasing mean IDP to 76% and 81% of baseline values at fractured and adjacent
5 levels, respectively. Injury also increased creep deformation of the vertebral body under
6 load, especially in the anterior region where a 14-fold increase was observed at the fractured
7 level and a three-fold increase at the adjacent level. Vertebroplasty reversed these changes
8 also, reducing deformation of the anterior vertebral body (compared to post-fracture values)
9 by 62% at the fractured level, and by 52% at the adjacent level.

10 **Conclusions:** Vertebral fracture adversely affects compressive load-sharing and increases
11 vertebral deformations at both fractured *and* adjacent levels. All effects can be partially
12 reversed by vertebroplasty.

13
14 **Keywords:** Vertebral fracture; vertebral deformity; vertebroplasty; adjacent level; intradiscal
15 pressure; cadaveric.

16
17 **Classification:** Basic science paper.

18

1 Introduction

2 Injury and degeneration often affect more than one spinal level. 'Adjacent-level' pathology
3 could be due to constitutional factors (such as genetic inheritance or ageing) leading to
4 concurrent changes at several spinal levels. Alternatively, changes at one spinal level could
5 have a direct biomechanical influence at adjacent levels, so that pathology spreads in a
6 'domino' effect, up or down the spine. This has important implications for the consequences
7 of injury at one spinal level.

8 Adjacent level effects are equally important when assessing the impact of therapeutic
9 interventions such as disc replacement,(1) spinal fusion and fixation,(2, 3) interspinous
10 implants,(4) and techniques such as vertebroplasty(5) which augment fractured vertebrae
11 with cement.(6-9) Approximately 50% of vertebral fractures that follow vertebroplasty affect
12 an adjacent vertebra,(10-12) suggesting a 'domino' effect. On the other hand, vertebroplasty
13 *reduces* the rate of adjacent-level fractures compared with conservative treatment,(9, 13)
14 suggesting that constitutional factors are important.(14-16)

15 Experiments on living subjects show that sagittal-plane mobility (and bending stiffness) can
16 be increased, decreased or remain the same at spinal levels that are adjacent to a fusion or to
17 advanced disc degeneration.(17, 18) In-vitro experiments attempting to explain these effects
18 also produce variable results which appear to depend on loading technique.(19) Changes in
19 *compressive* load-sharing at adjacent levels have been studied less, possibly because it is
20 more difficult to quantify than angular movements in bending. Vertebroplasty can reduce the
21 failure strength of adjacent vertebrae if a large volume (7-11 ml) of cement is injected,(5, 20)
22 presumably by increasing pressure in the adjoining disc nucleus(21) and increasing bulging
23 of the adjacent endplate.(22) Other studies, however, report that vertebroplasty does not
24 increase nucleus pressure right up to pre-fracture levels (23, 24) so that endplate deflection in

1 adjacent vertebrae is not increased.(25) This disagreement may be attributable to differences
2 in the volume and stiffness of bone cement used,(24, 26-30) with lower volumes of softer
3 cement likely to reduce the risk to adjacent levels. Further investigations are needed to clarify
4 the effects of fracture and surgical intervention on compressive load-sharing at adjacent
5 levels.

6 To understand how compressive load is transferred through the spine, we developed and
7 validated a technique for measuring compressive ‘stress’ across the mid-sagittal diameter of a
8 loaded intervertebral disc, as shown in Figure 1A.(31, 32) Multiplying the average stress on
9 each discrete region of the disc by the area of that region gives the compressive force on that
10 region, and summing these small forces (**Figure 1**) yields the total compressive force exerted
11 by the disc on the adjacent vertebral bodies. Subtracting this force from the applied
12 compressive load then indicates the compressive force resisted by the neural arch.(33) These
13 techniques have shown that vertebral body fracture transfers compressive loading from
14 nucleus to annulus, and from disc to neural arch, and that these effects can be partially
15 reversed by vertebroplasty.(24, 27, 34)

16 We have also developed a technique for assessing regional deformations of the vertebral
17 body under load, using a MacReflex optical strain measurement technique. Both elastic and
18 creep (time-dependent) deformations were greater anteriorly than posteriorly in older
19 spines.(35, 36) Deformations were increased following vertebral fracture, and decreased
20 following vertebroplasty.(37)

21 The present study will apply these techniques to answer the following questions. Does
22 vertebral body fracture affect compressive load-sharing and deformation in adjacent
23 vertebrae? And, does vertebroplasty make things worse, or better? Three-vertebra specimens
24 were used so that close comparisons could be made between fractured and adjacent spinal
25 levels in the same spine.

1

2 **Materials and methods**

3 *Experimental design* Each cadaver spine was dissected to obtain a matched pair of
4 specimens, each comprising three vertebrae and the intervening disc and ligaments. All
5 specimens were compressed until one of its vertebrae fractured. Fractured vertebrae were
6 treated by vertebroplasty, using either polymethylmethacrylate (PMMA) cement or an acrylic
7 resin, with the upper specimen from each spine being alternately assigned to receive one
8 treatment or the other. At each stage of the experiment (before fracture, after fracture and
9 following vertebroplasty) specimens were subjected to 1 hr of compressive loading during
10 which deformations of the vertebral bodies were evaluated optically. Intervertebral disc
11 stress distributions, and vertebral wedging, were measured before and after fracture, after
12 vertebroplasty, and following the final period of compressive loading which allowed
13 consolidation of the augmented vertebral body. Measurements were compared between each
14 stage of the experiment, and between the matched pair of specimens from each spine.

15 *Cadaveric material* Thoracolumbar spines (10 male, 4 female) were obtained from cadavers
16 aged 67-92 (mean 80) yrs which were donated for medical research. After storage at -20°C,
17 each spine was thawed at 3°C and dissected into two specimens comprising three vertebrae
18 with the intervening discs and ligaments. The 28 specimens ranged between T8-T10 and L2-
19 L4 (**Table 1**). Choice of spinal level was determined by the need to avoid large osteophytes
20 (which interfere with disc stress measurements) and to maximize the use of scarce human
21 tissue. Before testing, the bone mineral content (BMC) of each vertebral body was assessed
22 using dual energy X-ray absorptiometry.(27). After testing, vertebral bodies were dissected
23 and their volume measured by water displacement, for calculation of volumetric bone mineral
24 density (BMD). Each intervertebral disc was sectioned in the transverse plane and graded for

1 degeneration, using points 1 (non-degenerated) to 4 (severely degenerated) on a scale defined
2 previously.(38)

3 *Mechanical testing apparatus* Specimens were secured in cups of dental plaster and loaded
4 on a hydraulic materials testing machine (Dartec-Zwick-Roell, Leominster, UK). Low-
5 friction rollers of equal height were used to apply pure compression to specimens in a neutral
6 position (**Figure 2A**). This “neutral” position represents the natural angulation of the spinal
7 segment when no external forces are applied to it. By altering the height of the rollers
8 (**Figure 2B**), compression was also applied with each specimen flexed or extended relative to
9 its neutral position by angles that are typical of those seen in flexed and lordotic postures in-
10 vivo.(27)

11 *Vertebral fracture* Each specimen was positioned in moderate flexion to simulate a stooped
12 posture in life. Flexion angles ranged from 4° at thoracic levels to 10° at lower lumbar levels
13 to reflect natural variations in spinal flexibility. Specimens were then compressed at 3mm/s
14 until the load-deformation graph, recorded in real-time, indicated that the elastic limit had
15 been reached. This was marked by a reduction in gradient (stiffness). As soon as this
16 occurred, the compressive load was removed so that fracture severity would be slight, and
17 similar in all specimens. The force at the elastic limit was then recorded as the specimen’s
18 compressive strength. The location of fracture was confirmed from radiographs taken before
19 and after damage, and from dissection.

20 *Vertebroplasty* One of each pair of three-vertebra specimens was injected with PMMA
21 cement (Spineplex®, Stryker Instruments, Howmedica International, Limerick, Ireland) and
22 the other with an acrylic resin (Cortoss®, Orthovita, Malvern, PA, USA) as described
23 previously.(27) These cements differ in their material properties with PMMA having an
24 elastic modulus of approximately 2.26 GPa compared with 5.51 GPa for Cortoss.(39) Total
25 injected volume (through both pedicles) was 3.5 ml at spinal levels T7-T12, and 4 ml at L1-

1 L5, which is sufficient to largely restore normal stress distributions on fractured vertebral
2 bodies.(24) After injection, catheters and needles were removed from the vertebra, and the
3 cement was left to set for 1 hr. This was followed by a 1 hr period of compressive loading at
4 1 kN to encourage cement consolidation.

5 *Compressive stiffness* With each specimen positioned in slight flexion (4°), the compressive
6 force was increased at 500 N/s up to 1.0 kN, and then reduced to 50N. Compressive stiffness
7 of the three-vertebra specimen was measured (at each stage of the experiment) as the slope of
8 the load-deformation curve at 0.8 kN.

9 *Stress profilometry and compressive load-sharing* A miniature pressure transducer (Gaeltec,
10 Dunvegan, Scotland), side-mounted in a 1.3 mm diameter needle, was used to measure the
11 distribution of compressive “stress” along the mid-sagittal diameter of each intervertebral
12 disc (**Figure 1A**), while the specimen was compressed by 1.0 kN (20 specimens), 0.75 kN (5
13 specimens) or 0.5 kN (3 specimens), depending on its size and BMD. The pressure transducer
14 was attached to a linear variable displacement transducer (LVDT) which indicated the
15 position of the transducer within the disc. Readings from the LVDT were recorded
16 simultaneously with the pressure readings so that pressure could be plotted against distance
17 across the disc to produce a “stress profile” (**Figure 1A**). Stress profiles were recorded at
18 each stage of the experiment with the specimen positioned in slight extension (2°) to simulate
19 the ‘erect’ standing posture,(40) and again in $4^\circ - 6^\circ$ of flexion (depending on specimen
20 mobility) to simulate moderate flexion during light manual work.(41)

21 Stress profiles indicated the average intradiscal pressure (IDP) in the nucleus, and the size of
22 stress ‘peaks’ (concentrations) in the anterior (SP_A) and posterior (SP_P) annulus (**Figure 1A**).
23 Compressive load-bearing by anterior (F_A) and posterior (F_P) halves of the vertebral body
24 were determined by summing forces over discrete areas (**Figure 1B**). Compressive loading of

1 the neural arch (F_N) was then calculated by subtracting F_A and F_P from the applied
2 compressive force.(33)

3 *Vertebral body deformations* Prior to fracture, specimens were subjected to 1hr of
4 compressive loading at 1.0 kN to reduce intervertebral disc water content and height to
5 physiological levels (42) and to enable deformation of the intact vertebral bodies to be
6 evaluated.(35) The latter was assessed using a 2-D optical strain measurement system
7 (MacReflex, Qualisys Ltd., Goteborg, Sweden) that tracked the position of six reflective
8 markers attached to each vertebral body, at 50 Hz (**Figure 2**). Changes in the position of
9 these markers during sustained loading enabled vertical deformations of the anterior, middle
10 and posterior regions of the vertebral body to be assessed to an accuracy of 10 μ m.(43) The
11 present paper will consider only the relatively large “creep” deformations, which were
12 determined by subtracting the initial “elastic” deformation during application of the load from
13 the total vertical deformation over the 1 hr loading period.(44) Creep deformations were
14 measured before and after fracture, and again after vertebroplasty.

15 *Vertebral wedging* Specimens were loaded at 1kN in the neutral (erect) position while the
16 position of reflective markers attached to the vertebral body was determined using the
17 MacReflex (**Figure 2**). The vertical separation of markers placed on the anterior and posterior
18 vertebral body was used to calculate anterior and posterior vertebral height and hence
19 vertebral wedging. Changes in anterior and posterior vertebral body height, at each stage of
20 the experiment, were used to calculate residual anterior wedging of the vertebral body, which
21 is indicative of structural failure.(45, 46)

22 *Statistical analysis* BMD and degree of disc degeneration were compared in specimens in the
23 two cement groups using matched-pair t-tests. The effect of disc degeneration grade on
24 fracture type was examined using Fisher’s Exact test. Repeated measures analysis of
25 variance (ANOVA) was used to compare measurements following each intervention, with

1 'cement group' as a between-subject factor. Analyses were performed separately for fractured
2 and adjacent levels. Where a significant main effect was found, post-hoc paired comparisons
3 were used to identify where differences arose. Significance was accepted at $P < 0.05$. SPSS
4 v21.0[®] was used for statistical analysis.

5

6 **Results**

7 *Specimen details* These are summarised in **Table 1**. BMD ranged between 0.075 and 0.298
8 g/cm^3 . Disc degeneration grades were between 2 and 4 and never varied by more than one
9 grade point within an individual three-vertebra specimen. BMD and disc degeneration did
10 not differ significantly between the two cement groups. In the case of disc degeneration, this
11 was true when both average degeneration scores for each specimen and individual scores for
12 each disc were compared.

13 *Vertebral fracture* Radiographs revealed, in 17/28 specimens, that fracture occurred in the
14 uppermost (4/17) or lowermost (13/17) vertebra (**Figure 2A**), leaving two consecutive
15 vertebrae intact. The vertebra next to the fractured vertebra was designated an 'adjacent
16 vertebra' and the disc in between the two intact vertebrae was designated an 'adjacent disc'.
17 The other disc (next to the fractured vertebra) was designated an 'affected disc'. In 10
18 specimens, fracture occurred in the middle vertebra (**Figure 2B**) so both discs were 'affected'
19 and both vertebrae were 'adjacent'. In the remaining specimen, both the middle and lower
20 vertebrae were damaged, so both discs were 'affected' and the upper vertebra was 'adjacent'.
21 Consequently, a total of 29 vertebrae were fractured. Inspection of the radiographs, and
22 subsequent dissection, showed that 8/29 fractured vertebrae showed damage to the endplate
23 only, 9 suffered damage to the anterior cortex only, and 12 showed signs of damage to both
24 the anterior cortex and endplate (**Table 1, Figure 3B**). The type of fracture appeared to be

1 influenced by the degeneration grade of the adjacent disc ($P=0.05$) as follows: of 12 vertebrae
2 that sustained a fracture of both the endplate and anterior cortex, 8 were adjacent to grade 3
3 discs and none were adjacent to grade 4 discs; in contrast, fractures adjacent to grade 4 discs
4 always involved the anterior cortex only and not the endplate. In specimens where the
5 degeneration grade varied between the two discs, fracture occurred adjacent to the more
6 degenerated disc in 6 of these 7 cases.

7 *Vertebroplasty* Vertebroplasty was successfully completed in all specimens. Cement leakage
8 was observed in one specimen which received PMMA (**Table 1**).

9 *Compressive strength and stiffness* Vertebral compressive strength varied between 1.3 and
10 5.5 kN (**Table 1**). Fracture reduced compressive stiffness of the three-vertebra specimen to
11 62 (STD 19)% of the baseline (pre-fracture) value ($P<0.001$). Vertebroplasty increased
12 stiffness to 69 (STD 19)%, ($P<0.05$) but this remained lower than baseline ($P<0.05$).
13 Specimens in the two cement groups had similar strength and stiffness (**Table 1**).

14 *Stress profilometry and compressive load-sharing* Stress profile variables are summarised in
15 **Table 2**, which also indicates the statistical significance of observed changes. Transducer
16 damage during two tests meant that results could be analysed for only 36 'affected' and 16
17 'adjacent' discs. Cement type had no significant effect on stress profile results, so data from
18 both cement groups has been pooled for conciseness.

19 Comparisons of average values in **Table 2** show that vertebral fracture reduced IDP in
20 affected discs to 47% of baseline (in erect posture), and to 69% of baseline (in flexion). For
21 adjacent discs, the changes were less, with IDP falling to 73% and 88% of baseline,
22 respectively. Load-bearing by the anterior half of the vertebral body (F_A) of affected discs
23 also decreased after fracture, to 75% of baseline in erect posture, and to 74% in flexion.
24 Similar falls were seen in adjacent discs, with F_A decreasing to 75% and 64% of baseline in

1 erect and flexed postures respectively. Load-bearing by the posterior half of the vertebral
2 body (F_P) was little changed by fracture, in either affected or adjacent discs. The largest
3 changes were seen in the neural arch, where compressive load-bearing (F_N) increased after
4 fracture, to 134% of baseline in erect posture, and to 201% in flexed. Adjacent levels were
5 affected by a similar amount, with (F_N) increasing to 160% and 185% of baseline in erect and
6 flexed postures, respectively. Stress peaks in the annulus were very variable (**Table 2**), but
7 fracture increased them significantly in the posterior annulus (SP_P), regardless of posture, and
8 marginally decreased them in the anterior annulus (SP_A) in flexed posture. Similar but non-
9 significant changes in stress peaks occurred in adjacent discs.

10 Vertebroplasty partially reversed the fracture-induced reductions in IDP and F_A at the
11 affected level, usually raising them to within 70-90% of baseline values (**Table 2**).

12 Vertebroplasty also reduced stress peaks in the posterior annulus (SP_P) back towards baseline,
13 but had little effect on neural arch load bearing (F_N), which remained elevated. Some of the
14 effects of vertebroplasty were evident at the adjacent level (especially F_A) but to a reduced
15 extent. Consequently, changes at the adjacent level were not significant compared to post-
16 fracture values although they were sufficient to restore some measures to pre-fracture values
17 (**Table 2**). **Figure 4** compares the influence of fracture and vertebroplasty on IDP and F_A , at
18 affected and adjacent levels.

19 *Vertebral body deformations* Regional measures of creep deformation in the vertebral body
20 are shown in **Figure 5**. Cement type had no significant effect on these results so data from
21 both groups has been pooled. Before fracture, creep deformation was generally more marked
22 anteriorly when compared to middle and posterior regions, especially in the vertebral body
23 which subsequently fractured. Following fracture, creep deformation of the fractured
24 vertebral body increased significantly in all three regions, and these changes were fully or
25 partially reversed following vertebroplasty (**Figure 5**). Changes at adjacent levels, although

1 less marked, reflected those observed at the fractured level with values in middle and anterior
2 regions being fully restored to pre-fracture values following vertebroplasty.

3 *Vertebral wedging* MacReflex data showed that vertebral fracture increased anterior
4 wedging of the affected vertebral body ($P < 0.05$) from 0.33° (STD 0.47) to 0.94° (STD 0.92).
5 Wedging did not change significantly at 'adjacent' levels. Following vertebroplasty, anterior
6 wedging of the fractured vertebral body decreased marginally, from 0.94° to 0.78° ($P > 0.05$)
7 and this value remained unchanged following the final period of creep loading. Cement type
8 had no significant influence on these results.

9 **Discussion**

10 *Summary of findings* Compressive overload often damaged the anterior cortex as well as the
11 endplate, increasing anterior wedging of the vertebral body. These injuries reduced nucleus
12 pressure (IDP) and loading of the anterior vertebral body (F_A) at the injured level. In contrast,
13 stress concentrations in the posterior annulus (SP_P) and loading of the neural arch (F_N) were
14 substantially increased. Vertebroplasty partially reversed the changes in IDP, F_A and SP_P , and
15 in vertebral wedging, but had little effect on F_N . Changes at the adjacent level were similar to
16 those at the fractured level, but were reduced in magnitude, as indicated in **Figure 6**.

17 Fracture significantly increased vertebral body deformation at both fractured and adjacent
18 levels, and these changes were partially or fully reversed following vertebroplasty.

19 *Strengths and weaknesses of the study* A major strength is that complex loading was applied
20 to large human specimens, so that loading of the vertebral bodies by adjacent discs was
21 closely physiological. Consequently, induced vertebral fractures resembled those that occur
22 in living people,(47) involving damage to both the endplate and anterior cortex.(48) The use
23 of three-vertebra specimens also allowed compressive load distributions to be compared
24 between fractured and adjacent vertebrae in the same cadaveric spines. "Stress profilometry"

1 (49-51) and “stress integration” (33) have been extensively validated, and enable compressive
2 load-sharing to be quantified between nucleus and annulus, as well as between disc and
3 neural arch. Weaknesses of the study include the use of freeze-thawed cadaveric tissues
4 which are unsupported by spinal musculature. However, death and frozen storage have little
5 effect on the spine’s mechanical properties,(52, 53) and the loading apparatus was designed
6 to reproduce the combined action of gravity and stabilising muscle forces (54) in a manner
7 that prevents the spine ‘jack-knifing’ about the induced injury. Cadaveric studies are also
8 limited to evaluating short-term effects, raising the possibility that fracture-induced changes
9 may eventually be reversed. However, our previous cadaveric studies on osteoporotic spines
10 show that vertebral deformity does not reverse after fracture if the spine is loaded. On the
11 contrary, a small fracture-induced deformity progresses inexorably under load by a
12 combination of consolidation and accelerated ‘creep’ mechanisms.(43) Vertebroplasty can
13 reduce, but not eliminate, this progressive deformation.(37)

14 *Relationship to previous work* Endplate fracture is known to decompress the disc nucleus,(55)
15 increase load-bearing by the neural arch,(27, 56) and lead to anterior wedging of the vertebral
16 body.(48) Likewise, vertebroplasty partially reverses these changes,(24, 34) regardless of
17 cement type(27) or volume.(24) The novelty of the present study is that changes observed at
18 the injured level were mostly repeated (to a reduced extent) at adjacent (uninjured) levels.

19 Vertebral fracture has been reported to increase compressive strain in the anterior cortex of
20 adjacent vertebrae,(57, 58). Current results support these findings, with adjacent vertebrae
21 showing a 3-fold increase in creep deformation anteriorly (**Figure 5**). These increases occur
22 even though the proportion of the applied compressive load acting on the anterior half of the
23 adjacent disc is reduced (**Table 2**), suggesting that an increased proportion of the load is
24 transferred from trabecular bone to the cortex, at both fractured and adjacent levels.

1 Alternatively, it is possible that damage at the fractured level was accompanied by undetected
2 microdamage at neighbouring levels, which caused them to deform more under load.

3 In the present study, only 3.5-4 ml of cement were used in vertebroplasty, because large
4 cement volumes increase the risk of cement leakage(59) and may increase the risk of adjacent
5 level fracture without contributing to pain relief.(60) Small cement volumes may explain why
6 vertebroplasty did little to reduce neural arch load-bearing (**Table 2**). Previously, 7ml of
7 cement was shown to substantially unload the neural arch and restore the spine's compressive
8 stiffness.(24) For comparison, the volume of thoracolumbar vertebral bodies is approximately
9 15-35ml.(61)

10 *Explanation of results* Vertebral fracture often damages an endplate, allowing it to deform
11 more so that the disc nucleus is decompressed.(55) In older spines, the anterior cortex also
12 becomes susceptible to fracture because of osteoporotic changes which accompany disc
13 degeneration.(62) When discs are severely degenerated, the anterior vertebral body appears
14 to be the most likely site of fracture presumably because intradiscal pressure is too low to
15 fracture the endplate. Once damage occurs, some compressive load-bearing is shifted to the
16 annulus, and hence to the vertebral cortex and this may contribute to increased deformations
17 of the vertebral body, especially in the anterior cortex which is often damaged as a result of
18 compressive overload. Increased loading of the annulus causes it to bulge radially and lose
19 height, increasing compressive load-bearing by the neural arch. Anterior vertebral collapse
20 also shifts load-bearing from anterior to posterior, so that loading of the anterior vertebral
21 body (F_A) decreases while stress concentrations in the posterior annulus (SP_P) increase.
22 Increased neural arch load-bearing is substantially transmitted to adjacent levels via the
23 apophyseal joints, whose articular surfaces have only a thin covering of compliant cartilage to
24 separate adjacent bones. Changes in intra-discal stresses are also transmitted to adjacent
25 levels, but the effect is reduced by the relative deformability of intervertebral discs compared

1 to the bony apophyseal joints, which makes the anterior column much more compliant
2 (**Figure 4**). Vertebroplasty supports the damaged endplate and anterior cortex with injected
3 cement, reducing their deformation and hence reversing the above changes.

4 Overall, the results of this study support the concept of injury at one spinal level having a
5 direct biomechanical influence at adjacent levels, so that pathology spreads in a ‘domino’
6 effect. However, the results do not rule out the possibility that biological predisposition (via
7 genetic inheritance or ageing) can also promote degenerative changes at several spinal levels.

8 *Clinical significance* Vertebral body fracture shifts compressive load-bearing to the ‘posterior
9 column’ of neural arches, and a similar but reduced shift occurs at adjacent levels. This will
10 cause stress-shielding and (eventually) weakening of the anterior column of these
11 neighbouring vertebrae.(62, 63) Therefore, the results of this study can explain why vertebral
12 fracture increases the risk of subsequent fracture at adjacent levels.(14, 16, 64, 65) The fact
13 that vertebroplasty partially reverses this shift in load-bearing and also reduces vertebral body
14 deformation under load at both damaged *and* adjacent levels, suggests that the procedure is
15 beneficial rather than harmful to adjacent vertebrae. We found no evidence that injecting 3.5-
16 4 ml of cement increases disc stresses above baseline, at either the injured or adjacent levels,
17 in line with previous work.(23, 24, 27, 34) This could explain why patients treated with
18 vertebroplasty have a lower rate of adjacent level fracture compared with conservative
19 treatment.(9, 13)

20 *Unanswered questions and future research* Kyphoplasty (a modification of vertebroplasty) is
21 more effective at restoring vertebral body height and shape following fracture.(66) Future
22 research should examine whether kyphoplasty also has beneficial effects at adjacent spinal
23 levels.

1 **Acknowledgements:** We thank Clare Costigan for technical assistance. The study was
2 funded by a grant from Action Medical Research, U.K. Vertebroplasty materials and
3 equipment were provided by Orthovita and Stryker U.K.

4

Accepted Manuscript

1 References

- 2 1. Dmitriev AE, Cunningham BW, Hu N, Sell G, Vigna F, McAfee PC. Adjacent level
3 intradiscal pressure and segmental kinematics following a cervical total disc arthroplasty: an
4 in vitro human cadaveric model. *Spine*. 2005;30(10):1165-72.
- 5 2. Tan JS, Singh S, Zhu QA, Dvorak MF, Fisher CG, Oxland TR. The effect of cement
6 augmentation and extension of posterior instrumentation on stabilization and adjacent level
7 effects in the elderly spine. *Spine*. 2008;33(25):2728-40.
- 8 3. Mannion AF, Leivseth G, Brox JI, Fritzell P, Hagg O, Fairbank JC. ISSLS Prize
9 winner: Long-term follow-up suggests spinal fusion is associated with increased adjacent
10 segment disc degeneration but without influence on clinical outcome: results of a combined
11 follow-up from 4 randomized controlled trials. *Spine (Phila Pa 1976)*. 2014;39(17):1373-83.
- 12 4. Lindsey DP, Swanson KE, Fuchs P, Hsu KY, Zucherman JF, Yerby SA. The effects
13 of an interspinous implant on the kinematics of the instrumented and adjacent levels in the
14 lumbar spine. *Spine*. 2003;28(19):2192-7.
- 15 5. Berlemann U, Ferguson SJ, Nolte LP, Heini PF. Adjacent vertebral failure after
16 vertebroplasty. A biomechanical investigation. *J Bone Joint Surg Br*. 2002;84(5):748-52.
- 17 6. Barr JD, Barr MS, Lemley TJ, McCann RM. Percutaneous vertebroplasty for pain
18 relief and spinal stabilization. *Spine*. 2000;25(8):923-8.
- 19 7. Diamond TH, Bryant C, Browne L, Clark WA. Clinical outcomes after acute
20 osteoporotic vertebral fractures: a 2-year non-randomised trial comparing percutaneous
21 vertebroplasty with conservative therapy. *Med J Aust*. 2006;184(3):113-7.
- 22 8. Klazen CA, Lohle PN, de Vries J, Jansen FH, Tielbeek AV, Blonk MC, et al.
23 Vertebroplasty versus conservative treatment in acute osteoporotic vertebral compression
24 fractures (Vertos II): an open-label randomised trial. *Lancet*. 2010;376(9746):1085-92.

- 1 9. Farrokhi MR, Alibai E, Maghami Z. Randomized controlled trial of percutaneous
2 vertebroplasty versus optimal medical management for the relief of pain and disability in
3 acute osteoporotic vertebral compression fractures. *J Neurosurg Spine*. 2011;14(5):561-9.
- 4 10. Trout AT, Kallmes DF, Layton KF, Thielen KR, Hentz JG. Vertebral endplate
5 fractures: an indicator of the abnormal forces generated in the spine after vertebroplasty. *J*
6 *Bone Miner Res*. 2006;21(11):1797-802.
- 7 11. Voormolen MH, Lohle PN, Juttman JR, van der Graaf Y, Fransen H, Lampmann LE.
8 The risk of new osteoporotic vertebral compression fractures in the year after percutaneous
9 vertebroplasty. *J Vasc Interv Radiol*. 2006;17(1):71-6.
- 10 12. Lo YP, Chen WJ, Chen LH, Lai PL. New vertebral fracture after vertebroplasty. *J*
11 *Trauma*. 2008;65(6):1439-45.
- 12 13. Movrin I. Prevalence of adjacent-level fractures after osteoporotic vertebral
13 compression fractures: a prospective non-randomized trial comparing percutaneous
14 vertebroplasty with conservative therapy. *Acta Medico-Biotechnica*. 2011;4:34-44.
- 15 14. Silverman SL. The clinical consequences of vertebral compression fracture. *Bone*.
16 1992;13 Suppl 2:S27-31.
- 17 15. Ross PD, Genant HK, Davis JW, Miller PD, Wasnich RD. Predicting vertebral
18 fracture incidence from prevalent fractures and bone density among non-black, osteoporotic
19 women. *Osteoporos Int*. 1993;3(3):120-6.
- 20 16. Klotzbuecher CM, Ross PD, Landsman PB, Abbott TA, 3rd, Berger M. Patients with
21 prior fractures have an increased risk of future fractures: a summary of the literature and
22 statistical synthesis. *J Bone Miner Res*. 2000;15(4):721-39.
- 23 17. Malakoutian M, Volkheimer D, Street J, Dvorak MF, Wilke HJ, Oxland TR. Do in
24 vivo kinematic studies provide insight into adjacent segment degeneration? A qualitative
25 systematic literature review. *Eur Spine J*. 2015;24(9):1865-81.

- 1 18. Lee SH, Daffner SD, Wang JC, Davis BC, Alanay A, Kim JS. The change of whole
2 lumbar segmental motion according to the mobility of degenerated disc in the lower lumbar
3 spine: a kinetic MRI study. *Eur Spine J.* 2015;24(9):1893-900.
- 4 19. Volkheimer D, Malakoutian M, Oxland TR, Wilke HJ. Limitations of current in vitro
5 test protocols for investigation of instrumented adjacent segment biomechanics: critical
6 analysis of the literature. *Eur Spine J.* 2015;24(9):1882-92.
- 7 20. Fahim DK, Sun K, Tawackoli W, Mendel E, Rhines LD, Burton AW, et al. Premature
8 adjacent vertebral fracture after vertebroplasty: a biomechanical study. *Neurosurgery.*
9 2011;69(3):733-44.
- 10 21. Baroud G, Nemes J, Heini P, Steffen T. Load shift of the intervertebral disc after a
11 vertebroplasty: a finite-element study. *Eur Spine J.* 2003;12:421-6.
- 12 22. Polikeit A, Nolte LP, Ferguson SJ. The effect of cement augmentation on the load
13 transfer in an osteoporotic functional spinal unit: finite-element analysis. *Spine.*
14 2003;28(10):991-6.
- 15 23. Ananthakrishnan D, Berven S, Deviren V, Cheng K, Lotz JC, Xu Z, et al. The effect
16 on anterior column loading due to different vertebral augmentation techniques. *Clin Biomech*
17 (Bristol, Avon). 2005;20(1):25-31.
- 18 24. Luo J, Daines L, Charalambous A, Adams MA, Annesley-Williams DJ, Dolan P.
19 Vertebroplasty: only small cement volumes are required to normalize stress distributions on
20 the vertebral bodies. *Spine (Phila Pa 1976).* 2009;34(26):2865-73.
- 21 25. Hulme PA, Boyd SK, Heini PF, Ferguson SJ. Differences in endplate deformation of
22 the adjacent and augmented vertebra following cement augmentation. *Eur Spine J.*
23 2009;18(5):614-23.
- 24 26. Baroud G, Bohner M. Biomechanical impact of vertebroplasty. Postoperative
25 biomechanics of vertebroplasty. *Joint Bone Spine.* 2006;73(2):144-50.

- 1 27. Luo J, Skrzypiec DM, Pollintine P, Adams MA, Annesley-Williams DJ, Dolan P.
2 Mechanical efficacy of vertebroplasty: Influence of cement type, BMD, fracture severity, and
3 disc degeneration. *Bone*. 2007;40(4):1110-9.
- 4 28. Chevalier Y, Pahr D, Charlebois M, Heini P, Schneider E, Zysset P. Cement
5 distribution, volume, and compliance in vertebroplasty: some answers from an anatomy-
6 based nonlinear finite element study. *Spine*. 2008;33(16):1722-30.
- 7 29. Nouda S, Tomita S, Kin A, Kawahara K, Kinoshita M. Adjacent vertebral body
8 fracture following vertebroplasty with polymethylmethacrylate or calcium phosphate cement:
9 biomechanical evaluation of the cadaveric spine. *Spine (Phila Pa 1976)*. 2009;34(24):2613-8.
- 10 30. Boger A, Heini P, Windolf M, Schneider E. Adjacent vertebral failure after
11 vertebroplasty: a biomechanical study of low-modulus PMMA cement. *Eur Spine J*.
12 2007;16(12):2118-25.
- 13 31. McNally DS, Adams MA. Internal intervertebral disc mechanics as revealed by stress
14 profilometry. *Spine*. 1992;17(1):66-73.
- 15 32. Adams MA, McNally DS, Dolan P. 'Stress' distributions inside intervertebral discs.
16 The effects of age and degeneration. *J Bone Joint Surg Br*. 1996;78(6):965-72.
- 17 33. Pollintine P, Przybyla AS, Dolan P, Adams MA. Neural arch load-bearing in old and
18 degenerated spines. *J Biomech*. 2004;37(2):197-204.
- 19 34. Farooq N, Park JC, Pollintine P, Annesley-Williams DJ, Dolan P. Can vertebroplasty
20 restore normal load-bearing to fractured vertebrae? *Spine*. 2005;30(15):1723-30.
- 21 35. Pollintine P, Luo J, Offa-Jones B, Dolan P, Adams MA. Bone creep can cause
22 progressive vertebral deformity. *Bone*. 2009;45(3):466-72.
- 23 36. Luo J, Pollintine P, Gomm E, Dolan P, Adams MA. Vertebral deformity arising from
24 an accelerated "creep" mechanism. *Eur Spine J*. 2012;21(9):1684-91.

- 1 37. Luo J, Pollintine P, Annesley-Williams DJ, Dolan P, Adams MA. Vertebroplasty
2 reduces progressive 'creep' deformity of fractured vertebrae. *Journal of Biomechanics*.
3 2016;49(6):869-74.
- 4 38. Adams M, Dolan P, Hutton W. The stages of disc degeneration as revealed by
5 discograms. *J Bone Joint Surg Br*. 1986;68-B(1):36-41.
- 6 39. Jasper LE, Deramond H, Mathis JM, Belkoff SM. Material properties of various
7 cements for use with vertebroplasty. *J Mater Sci Mater Med*. 2002;13(1):1-5.
- 8 40. Adams MA, Hutton WC. The effect of posture on the role of the apophysial joints in
9 resisting intervertebral compressive forces. *J Bone Joint Surg [Br]*. 1980;62(3):358-62.
- 10 41. Dolan P, Earley M, Adams MA. Bending and compressive stresses acting on the
11 lumbar spine during lifting activities. *J Biomech*. 1994;27(10):1237-48.
- 12 42. McMillan DW, Garbutt G, Adams MA. Effect of sustained loading on the water
13 content of intervertebral discs: implications for disc metabolism. *Ann Rheum Dis*.
14 1996;55(12):880-7.
- 15 43. Green TP, Allvey JC, Adams MA. Spondylolysis. Bending of the inferior articular
16 processes of lumbar vertebrae during simulated spinal movements. *Spine*. 1994;19(23):2683-
17 91.
- 18 44. Pollintine P, van Tunen MS, Luo J, Brown MD, Dolan P, Adams MA. Time-
19 dependent compressive deformation of the ageing spine: relevance to spinal stenosis. *Spine*
20 (Phila Pa 1976). 2010;35(4):386-94.
- 21 45. Zebaze RM, Maalouf G, Maalouf N, Seeman E. Loss of regularity in the curvature of
22 the thoracolumbar spine: a measure of structural failure. *J Bone Miner Res*. 2004;19(7):1099-
23 104.

- 1 46. Pettersen PC, de Bruijne M, Chen J, He Q, Christiansen C, Tanko LB. A computer-
2 based measure of irregularity in vertebral alignment is a BMD-independent predictor of
3 fracture risk in postmenopausal women. *Osteoporos Int.* 2007;18(11):1525-30.
- 4 47. Jiang G, Luo J, Pollintine P, Dolan P, Adams MA, Eastell R. Vertebral fractures in
5 the elderly may not always be "osteoporotic". *Bone.* 2010;47(1):111-6.
- 6 48. Landham PR, Gilbert SJ, Baker-Rand HL, Pollintine P, Robson Brown KA, Adams
7 MA, et al. Pathogenesis of Vertebral Anterior Wedge Deformity: A 2-Stage Process? *Spine*
8 (Phila Pa 1976). 2015;40(12):902-8.
- 9 49. Chu JY, Skrzypiec D, Pollintine P, Adams MA. Can compressive stress be measured
10 experimentally within the annulus fibrosus of degenerated intervertebral discs? *Proc Inst*
11 *Mech Eng [H].* 2008;222(2):161-70.
- 12 50. McMillan DW, McNally DS, Garbutt G, Adams MA. Stress distributions inside
13 intervertebral discs: the validity of experimental 'stress profilometry'. *Proc Inst Mech Eng*
14 *[H].* 1996;210(2):81-7.
- 15 51. McNally DS, Adams MA, Goodship AE. Development and validation of a new
16 transducer for intradiscal pressure measurement. *J Biomed Eng.* 1992;14(6):495-8.
- 17 52. Adams M, Bogduk N, Burton K, Dolan P. *The Biomechanics of Back Pain* (3rd
18 Edition). Churchill Livingstone, Edinburgh; 2013.
- 19 53. Adams MA. Mechanical testing of the spine. An appraisal of methodology, results,
20 and conclusions. *Spine.* 1995;20(19):2151-6.
- 21 54. Adams MA, Hutton WC, Stott JR. The resistance to flexion of the lumbar
22 intervertebral joint. *Spine.* 1980;5(3):245-53.
- 23 55. Dolan P, Luo J, Pollintine P, Landham PR, Stefanakis M, Adams MA. Intervertebral
24 disc decompression following endplate damage: implications for disc degeneration depend on
25 spinal level and age. *Spine (Phila Pa 1976).* 2013;38(17):1473-81.

- 1 56. Adams MA, Freeman BJ, Morrison HP, Nelson IW, Dolan P. Mechanical initiation of
2 intervertebral disc degeneration. *Spine*. 2000;25(13):1625-36.
- 3 57. Kayanja MM, Ferrara LA, Lieberman IH. Distribution of anterior cortical shear strain
4 after a thoracic wedge compression fracture. *Spine J*. 2004;4(1):76-87.
- 5 58. Tzermiadianos MN, Renner SM, Phillips FM, Hadjipavlou AG, Zindrick MR, Havey
6 RM, et al. Altered disc pressure profile after an osteoporotic vertebral fracture is a risk factor
7 for adjacent vertebral body fracture. *Eur Spine J*. 2008;17:1522-30.
- 8 59. Ryu KS, Park CK, Kim MC, Kang JK. Dose-dependent epidural leakage of
9 polymethylmethacrylate after percutaneous vertebroplasty in patients with osteoporotic
10 vertebral compression fractures. *J Neurosurg*. 2002;96(1 Suppl):56-61.
- 11 60. Jin YJ, Yoon SH, Park KW, Chung SK, Kim KJ, Yeom JS, et al. The volumetric
12 analysis of cement in vertebroplasty: relationship with clinical outcome and complications.
13 *Spine (Phila Pa 1976)*. 2011;36(12):E761-72.
- 14 61. Limthongkul W, Karaikovic EE, Savage JW, Markovic A. Volumetric analysis of
15 thoracic and lumbar vertebral bodies. *Spine J*. 2010;10(2):153-8.
- 16 62. Adams MA, Pollintine P, Tobias JH, Wakley GK, Dolan P. Intervertebral disc
17 degeneration can predispose to anterior vertebral fractures in the thoracolumbar spine. *J Bone
18 Miner Res*. 2006;21(9):1409-16.
- 19 63. Adams MA, Dolan P. Biomechanics of vertebral compression fractures and clinical
20 application. *Arch Orthop Trauma Surg*. 2011;131(12):1703-10.
- 21 64. Melton LJ, 3rd, Atkinson EJ, Cooper C, O'Fallon WM, Riggs BL. Vertebral fractures
22 predict subsequent fractures. *Osteoporos Int*. 1999;10(3):214-21.
- 23 65. Lindsay R, Silverman SL, Cooper C, Hanley DA, Barton I, Broy SB, et al. Risk of
24 new vertebral fracture in the year following a fracture. *JAMA*. 2001;285(3):320-3.

1 66. Landham PR, Baker-Rand HL, Gilbert SJ, Pollintine P, Annesley-Williams DJ,
2 Adams MA, et al. Is kyphoplasty better than vertebroplasty at restoring form and function
3 after severe vertebral wedge fractures? *Spine J.* 2015;15(4):721-32.

4
5 **Figure 1. (A)** Typical ‘stress profile’ indicating the intradiscal pressure (IDP), and the peak
6 compressive stress in the anterior (SP_A) and posterior (SP_P) annulus. **(B)** To calculate the
7 total compressive force acting on the disc from the stress profile, anterior and posterior halves
8 of the disc were each modelled as a series of semi-elliptical strips of known area. The
9 compressive force acting on the N^{th} anterior strip (F_{AN}) was quantified by multiplying its area
10 (S_N) by the average stress on this strip (P_{AN}) taken from the stress profile. The same
11 procedure was carried out for all posterior and anterior strips. These individual small forces
12 were summed to give the compressive force acting on the anterior (F_A) and posterior (F_P)
13 halves of the disc. The compressive force acting on the neural arch (F_N) was then obtained
14 by subtracting F_A and F_P from the known force applied to the specimen. Adapted from
15 Pollintine et al. (33).

16 **Figure 2.** Each three-vertebra specimen was secured in cups of dental plaster and compressed
17 by two low-friction rollers, the height of which could be altered to simulate “neutral”
18 postures, where no bending was applied (A), or “flexed” postures (B). If fracture was induced
19 in the lowest vertebra (X), and the other two were unfractured (U), then the disc between the
20 middle and lowest vertebrae was designated the ‘affected’ disc, and the disc between the two
21 upper vertebrae was termed ‘adjacent’, as depicted in (A). Equivalent terminology was used
22 if the uppermost vertebra was fractured. If the middle vertebra was fractured, then both discs
23 were considered to be ‘affected’ as depicted in (B).

1 **Figure 3.** Radiographs of a cadaveric specimen (Male, 92 yrs, T11-L1) taken before (A) and
2 after (B) fracture. The block arrow indicates where the main fracture plane meets the anterior
3 cortex.

4 **Figure 4.** Effects of vertebral fracture and vertebroplasty on 'affected' and 'adjacent' discs.
5 A) Nucleus pressure (IDP) decreases following vertebral fracture, and increases following
6 vertebroplasty, at both affected and adjacent levels. Data refers to erect posture. B) Loading
7 of the anterior vertebral body (FA), expressed as a percent of the total applied load, decreases
8 following vertebral fracture, and increases following vertebroplasty, at both affected and
9 adjacent levels. Data refer to flexed posture. Significant differences between pre- and post-
10 fracture values are denoted * ($P<0.05$), ** ($P<0.01$) and *** ($P<0.001$). Significant
11 differences between post-fracture and either post-vertebroplasty or post-consolidation values
12 are denoted + ($P<0.05$), ++ ($P<0.001$) and +++ ($P<0.001$). Error bars indicate the SEM.

13 **Figure 5.** Vertebral fracture and vertebroplasty affect creep deformation of fractured and
14 adjacent vertebral bodies. Measurements were made pre-fracture (Pre_X), post-fracture
15 (Post_X) and post-vertebroplasty (Post_VP) in the posterior, middle and anterior cortex of
16 each vertebral body. Significant differences between pre- and post-fracture values are
17 denoted * ($P<0.05$), ** ($P<0.01$) and *** ($P<0.001$). Significant differences between post-
18 fracture and post-vertebroplasty values are denoted † ($P<0.05$), †† ($P<0.001$) and †††
19 ($P<0.001$). Error bars indicate the SEM.

20 **Figure 6.** Cartoon illustrating how vertebral fracture alters compressive load-sharing at the
21 fractured and adjacent levels. As indicated by the size of the arrows, fracture transfers loading
22 from the central vertebral body to the vertebral cortex, and to the neural arch. The adjacent
23 level is similarly affected, but to a reduced extent. Vertebroplasty partially reverses these
24 changes. Note that vertebral fracture increased anterior wedging of the vertebral body by only
25 0.61 degrees on average.

1

2 **Table 1. Details of the 14 pairs of specimens tested**

Spine	Gender	Age (years)	Spinal level		Disc Degeneration#		BMD (g/cm ³) ⁺		Yield strength (kN)		Compressive stiffness (kN/mm)		Fracture type	
			C	P	C	P	C	P	C	P	C	P	C	P
1	Female	87	T9-T11	T1-L2	4:4	3:3	0.075	0.077	1.5	1.5	1.60	0.42	AC	EP
2	Male	90	T10-T12	L2-L4	3:3	3:2	0.086	0.129	1.5	1.9	0.82	0.87	EP+AC	EP+AC
3	Male	79	L2-L4	T1-L1	2:2	3:3	0.298	0.270	4.7	5.5	1.49	2.57	EP	EP
4	Male	71	T1-L1	T8-T10	2:3	3:3	0.270	0.172	2.8	2.5	1.98	3.17	EP+AC	EP+AC†
5	Male	67	T1-L1	L2-L4	2:3	2:2	0.261	0.267	3	4.9	2.15	1.42	EP+AC	EP+AC
6	Female	81	L1-L3	T10-T12*	2:2	3:3	0.122	0.097	1.3	1.6	0.78	2.08	EP+AC	EP+AC
7	Male	83	T1-L1	L2-L4	3:3	3:3	0.205	0.175	2.2	2.9	1.67	1.39	EP	EP+AC
8	Male	92	T1-L1	T8-T10	4:4	4:3	0.090	0.089	1.9	1.5	1.42	1.24	AC	AC
9	Female	85	L2-L4	T1-L1	3:3	2:2	0.199	0.200	3.1	1.4	1.90	1.12	EP	EP+AC
10	Male	78	T1-L1	L2-L4	3:2	3:3	0.153	0.178	3.6	3.5	1.85	1.39	AC	AC
11	Male	76	T10-T12	L2-L4	3:4	3:3	0.138	0.237	2.0	2.4	1.45	0.89	AC	AC
12	Female	68	L2-L4	T1-L1	2:2	2:2	0.162	0.136	3.2	3.8	1.25	2.14	AC	EP+AC
13	Male	83	T10-L3	L1-L3	2:2	3:3	0.135	0.269	3.3	3.9	2.19	1.94	EP	EP

Effect of vertebral fracture on adjacent levels

14	Male	82	T1 2 L1- L3	T1 0- T1 2	3:2	2:2	0.122	0.108	2.3	1.9	0.99	1.75	EP	AC
Mean (SD)		80 (8)					0.165 (0.07 1)	0.172 (0.06 9)	2.6 (0. 9)	2.8 (1. 4)	1.54 (0.4 6)	1.60 (0.7 3)		

1

2 Note: The cement used for vertebroplasty is denoted as follows: C, Cortoss; P, PMMA. # Grade of disc
3 degeneration is shown for the upper (U) and lower (L) discs of each three-vertebra specimen. + Volumetric
4 BMD values are those of the fractured vertebra. * Cement leakage observed during vertebroplasty (leakage
5 volume 1 ml). Fracture types defined as endplate (EP), anterior cortex (AC) or endplate plus anterior cortex
6 (EP+AC). †In this specimen, two vertebrae sustained fracture of the endplate and anterior cortex.

Accepted Manuscript

1 **Table 2.** Average (SD) results in flexed and erect posture for 36 ‘affected’ and 16 ‘adjacent’ discs. P values indicate main effects across the four stages of
 2 the experiment (ANOVA). Post-hoc paired comparisons indicate differences from pre-fracture (^a p < 0.05; ^b p < 0.01; ^c p < 0.001) and post-fracture (^A p <
 3 0.05; ^B p < 0.01; ^C p < 0.001) values. Post-consolidation measurements were obtained following a 1 hr period of compressive loading at 1 kN following
 4 vertebroplasty to allow cement consolidation. Intradiscal pressure in the nucleus (IDP) and the size of stress peaks in the anterior (SP_A) and posterior (SP_P)
 5 annulus are given in megapascals (MPa).

		Pre-fracture	Post-fracture	Post-vertebroplasty	Post-consolidation	P
IDP- flexed (MPa)	Affected	0.80 (0.47)	0.55 (0.30) ^c	0.70 (0.34) ^C	0.66 (0.31) ^{bC}	<0.001
	Adjacent	0.90 (0.45)	0.78 (0.44) ^a	0.79 (0.50)	0.76 (0.45) ^a	0.016
IDP- erect (MPa)	Affected	0.75 (0.40)	0.35 (0.28) ^c	0.57 (0.29) ^{cC}	0.53 (0.28) ^{cC}	<0.001
	Adjacent	0.94 (0.39)	0.70 (0.51) ^b	0.76 (0.53) ^{aA}	0.72 (0.47) ^b	0.003
SP _A – flexed (MPa)	Affected	1.39 (1.17)	1.10 (0.66) ^a	1.17 (0.94)	1.26 (0.97) ^A	0.166
	Adjacent	1.58 (1.87)	0.81 (1.35)	0.90 (1.09)	1.20 (1.51)	0.120
SP _A – erect (MPa)	Affected	0.60 (0.58)	0.70 (0.49)	0.75 (0.56)	0.63 (0.48)	0.158
	Adjacent	0.62 (0.77)	0.44 (0.72)	0.52 (0.58)	0.44 (0.54)	0.457
SP _P - flexed (MPa)	Affected	0.45 (0.67)	0.86 (0.82) ^b	0.42 (0.49) ^C	0.41 (0.49) ^C	0.001
	Adjacent	0.22 (0.38)	0.76 (0.88)	0.39 (0.55) ^a	0.40 (0.54) ^a	0.109
SP _P - erect (MPa)	Affected	0.69 (0.73)	1.52 (1.09) ^c	0.92 (0.70) ^C	0.95 (0.77) ^C	<0.001
	Adjacent	0.85 (1.01)	1.17 (0.87)	0.92 (0.74)	0.84 (0.64)	0.431
F _A - flexed (%)	Affected	55.2 (17.4)	40.7 (11.7) ^c	46.9 (14.4) ^{aB}	46.3 (13.0) ^{bB}	<0.001

	Adjacent	55.5 (21.5)	35.6 (15.1) ^a	42.4 (14.0) ^a	45.5 (19.0)	0.003
F _A - erect (%)	Affected	35.3 (13.1)	26.3 (13.2) ^c	30.4 (11.8) ^{aA}	29.1 (11.9) ^{cA}	<0.001
	Adjacent	37.1 (16.3)	27.9 (15.3) ^b	31.4 (12.5) ^a	30.2 (12.6) ^a	0.007
F _P - flexed (%)	Affected	31.4 (14.0)	32.4 (14.3)	29.3 (12.7)	26.6 (11.5) ^{bb}	0.005
	Adjacent	28.1 (13.5)	34.1 (15.4)	28.3 (16.2)	27.7 (15.4)	0.148
F _P - erect (%)	Affected	37.2 (14.8)	35.2 (16.9)	34.7 (15.2)	35.2 (16.7)	0.618
	Adjacent	39.5 (11.8)	38.7 (19.3)	35.6 (17.4)	34.4 (15.1)	0.162
F _N - flexed (%)	Affected	13.4 (14.3)	26.9 (16.1) ^c	23.8 (15.8) ^a	27.1 (13.8) ^c	<0.001
	Adjacent	16.4 (16.9)	30.3 (15.9) ^a	29.3 (17.8) ^a	26.9 (18.8) ^a	0.022
F _N - erect (%)	Affected	28.6 (16.9)	38.2 (21.2) ^b	34.8 (17.9) ^a	36.1 (21.2) ^a	0.011
	Adjacent	21.4 (18.4)	34.3 (24.2) ^b	33.7 (22.7) ^a	34.7 (21.1) ^b	0.001

1

2

3