Application of digital volume correlation to study the efficacy of prophylactic vertebral augmentation

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1 **ABSTRACT**

2 **Background** – Prophylactic augmentation is meant to reinforce the vertebral body, but in
3 some cases it is suspected to actually weaken it. Past studies only investigated structural
4 failure and the surface strain distribution. To elucidate the failure mechanism of the
5 augmented vertebra, more information is needed about the internal strain distribution. This
6 study aims to measure, for the first time, the full-field three-dimensional strain distribution
7 inside augmented vertebrae in the elastic regime and to failure.

8 **Methods** – Eight porcine vertebrae were prophylactically-augmented using two augmentation
9 materials. They were scanned with a micro-computed tomography scanner (38.8micrometer
10 voxel resolution) while undeformed, and loaded at 5%, 10%, 15% compression. Internal
11 strains (axial, antero-posterior and lateral-lateral components) were computed using digital
12 volume correlation.

13 **Findings** – For both augmentation materials, the highest strains were measured in the regions
14 adjacent to the injected cement mass, whereas the cement-interdigitated-bone was less
15 strained. While this was already visible in the elastic regime (5%), it was a predictor of the
16 localization of failure, which became visible at higher degrees of compression (10% and
17 15%), when failure propagated across the trabecular bone. Localization of high strains and
18 failure was consistent between specimens, but different between the cement types.

19 **Interpretation** – This study indicated the potential of digital volume correlation in measuring
20 the internal strain (elastic regime) and failure in augmented vertebrae. While the cement-
21 interdigitated region becomes stiffer (less strained), the adjacent non-augmented trabecular
22 bone is affected by the stress concentration induced by the cement mass. This approach can
23 help establish better criteria to improve vertebroplasty.

24 **Keywords:**

25 Prophylactic vertebral augmentation; Digital volume correlation; Cement-bone interface;
26 Bone fracture; Micro-damage; Full-field three-dimensional strain measurement

27

1. INTRODUCTION

Vertebral fractures are a severe cause of morbidity and disability (Ferrar et al., 2005; Tancioni et al., 2011), as well as a significant burden for healthcare systems (Goldstein et al., 2015). The cause of the fracture may be pathological, traumatic, or a combination of the two. The main pathological conditions are osteoporosis (WHO, 2007) and metastatic lesions (Sutcliffe et al., 2013), which are associated with metabolic alterations resulting in bone weakening. However, the biomechanics underlying fracture onset and development of post-fracture and prophylactic treatments raises research questions that are still far from being answered.

Recently, prophylactic augmentation (cement injection in a non-fractured vertebra) has been proposed as an alternative to pharmacological treatments (Diamond et al., 2003) to reduce the fracture risk of osteoporotic vertebrae (Chiang et al., 2009; Kayanja et al., 2005; Langdon et al., 2009; Sun and Liebschner, 2004; Tancioni et al., 2011), or to prevent adjacent fractures after augmentation (Aquarius et al., 2014; Kobayashi et al., 2009). This treatment is meant to increase the strength and the structural support of weak vertebrae, by the injection of an augmentation material into the vertebral body (Aquarius et al., 2014; Chiang et al., 2009; Cristofolini et al., 2016; Oakland et al., 2008; Oakland et al., 2009; Sun and Liebschner, 2004).

Questions have been raised about the efficacy and safety of vertebroplasty in general, because of the associated risks such as cement leakage and subsequent neural damage; tissue necrosis due to residual monomer and to the exothermal reaction; increased risk of fracture in the adjacent vertebrae (Berlemann et al., 2002; Carrodeguas et al., 2004; Lewis, 2006; Tanigawa et al., 2006; Uppin et al., 2003). Prophylactic augmentation exposes the patients to such risks; hence there is a need for a clearer understanding on the cost-benefit trade-off. For this reason, in-depth knowledge of the mechanical behaviour and failure of augmented vertebra is of fundamental importance to understand vertebral biomechanics and improve diagnosis and prophylactic treatments (Oakland et al., 2008).

Furthermore, it is still debated whether prophylactic augmentation actually strengthens the treated vertebra. The increasing interest in the use of prophylactic augmentation, as a treatment for reduce the risk of fracture, has led to a number of experimental studies (Belkoff et al., 2001; Cristofolini et al., 2016; Heini et al., 2001; Ikeuchi et al., 2001; Kolb et al., 2013; Kruger et al., 2013; Lewis et al., 2008; Lim et al., 2002; Molloy et al., 2005; Rotter et al.,

2015; Steens et al., 2007; Tohmeh et al., 1999; Wilke et al., 2006). Several *in vitro* studies showed that the strength of augmented vertebrae was on average greater than that of non-augmented vertebrae (Ikeuchi et al., 2001; Lim et al., 2002). However, there were also cases where single treated specimens were weaker than the untreated controls (Berlemann et al., 2002; Dean et al., 2000). In fact, augmentation has been found to strengthen (Bai et al., 1999; Higgins et al., 2003; Lim et al., 2002), to provide no improvement (Kayanja et al., 2005), or even to weaken at least some specimens (Berlemann et al., 2002; Widmer Soyka et al., 2016), in comparison to untreated controls. It must be noted that most of these studies focused on the overall failure strength of the natural and treated vertebral body, without analyzing the strain distribution.

The strain distribution has been partially assessed in the untreated vertebral body (Kayanja et al., 2004) (the most stressed region could not be identified as only one strain-gauge was applied on each vertebra). Recently, the strain distribution was measured for a variety of loading conditions with a large number (8) of strain gauges (Cristofolini et al., 2013). While strain gauges provide point-wise measurements, digital image correlation (DIC) allows for the investigation of full-field strain distribution on the surface of the specimen. In recent years, DIC has been successfully exploited to measure the strain distribution on the surface of untreated vertebrae (Campos-Lopez et al., 2015; Giambini, 2013; Grassi and Isaksson, 2015; Palanca et al., 2015a; Palanca et al., 2016). The surface strain distribution was also measured in augmented vertebrae *in vitro*, using 8 strain gauges (Cristofolini et al., 2016). The measured principal strains were generally aligned as expected: axially/circumferentially for all loading conditions, implying an axial force. It has been shown both experimentally (Cristofolini et al., 2016) and numerically (Widmer Soyka et al., 2016) that the variability of the weakening/strengthening effect depends on the quality of augmentation (amount, localization and distribution of the injected material). Even that study could not draw any conclusive information about the failure mechanisms associated to the internal state of the vertebra.

Numerical predictions through finite element (FE) models allowed the investigation of the internal strain distribution (e.g. (Kinzl et al., 2013; Sun and Liebschner, 2004; Wilcox, 2006)). However, FE models of complex structures such as an augmented vertebra, which include a thin cortical shell, cement-bone interdigitation, tissue anisotropy, inhomogeneity and nonlinearity must be first verified and then validated (Cristofolini et al., 2010; Henninger et al., 2010).

With the recent and rapid progress of high-resolution micro-CT imaging in conjunction with *in situ* mechanical testing (Buffière et al., 2010; Nazarian and Muller, 2004), digital volume correlation (DVC) emerged as a novel tool for the measurement of 3D deformation fields throughout entire bone volumes (Freddi et al., 2015; Roberts et al., 2014). So far, DVC has been successfully employed to examine full-field internal deformations in trabecular bone (Bay et al., 1999; Brémand F., 2008; Dall'Ara et al., 2014; Gillard et al., 2014; Liu and Morgan, 2007; Zauel et al., 2006), cortical bone (Christen et al., 2012; Dall'Ara et al., 2014; Palanca et al., 2015b) and cement-bone interface (Tozzi et al., 2014). Application of DVC to whole untreated vertebra was also exploited to examine yield and post-yield deformations (Hussein et al., 2012; Hussein et al., 2013). DVC is an ideal tool to investigate the internal mechanism leading to failure onset and progression in augmented vertebrae, and could potentially be used to elucidate under which conditions augmentation can reinforce/weaken the vertebral body.

While DVC has been applied to characterize the mechanical performance of untreated vertebral body, so far it has not been applied to augmented vertebral bodies. Recently, for the first time, 3D zero-strain studies demonstrated the suitability of DVC to investigate augmented vertebrae both at organ and tissue level (Tozzi et al., 2015). This study reported that strain uncertainties can be reduced below 300 microstrain if the images are adequately prepared (excluding the non-tissue background), and with an appropriate choice of the computation sub-volume size (i.e. 48 voxels for a 39 micrometers voxel size image).

The aim of this study was to use DVC, for the first time, to improve the understanding of the failure mechanism inside prophylactically-augmented vertebral bodies. DVC was applied to measure the full-field strain distribution under compression inside the vertebral body augmented with two different cements. The approach enabled focusing on the injected cement, and on the cement-bone interdigitated region, in the immediate post-operative period. The investigation included both the elastic regime (axial, antero-posterior and lateral-lateral components of strain) and the yield/failure internal micro-damage mechanism.

2. METHODS

2.1 Specimens and prophylactic augmentation

Four porcine thoracic spine segments (T1-T3) were obtained from animals sacrificed for alimentary purposes. The animals were all female, of the same breed, approximately 9

months old and 100kg at sacrifice. The single vertebrae were dissected, removing the soft tissues, including the intervertebral discs (Fig.1). The vertebral bodies measured 20.0-24.0 mm in the cranial-caudal, 18.0-20.5 mm in the antero-posterior, and 26.1-31.3 mm in the lateral-lateral direction. They were treated with two vertebral augmentation materials:

- Four vertebrae (Mendec-1, Mendec-2, Mendec-3, Mendec-4) were prophylactically-augmented with an acrylic cement (Mendec-Spine, Tecres, Verona Italy). Mendec-Spine contains 20.4% BaSO₄ pellets with an average size of 300 micrometers, which grant adequate visibility during micro-CT imaging (Tozzi et al., 2015).
- Four vertebrae (Calcemex-1, Calcemex-2, Calcemex-3, Calcemex-4) were treated with an acrylic-based cement (Calcemex-Spine, Tecres). Calcemex-Spine contains 26% beta-tri-calcium-phosphate (β -TCP), and 6.5% BaSO₄ pellets with an average size of 300 micrometers.

Augmentation was performed using a unilateral approach (Fig.1) using the proprietary mixing and delivery kit. Injection was stopped at the first visible sign of leakage (injected volume: 1.0-1.5 ml of cement). In order to facilitate a more realistic flow and polymerization of the augmentation material, the vertebrae were placed in saline solution at 42°C 1 hour before and 12 hours after augmentation (the physiologic temperature in pigs is 39-41°C (Reece, 2004; Ye et al., 2007)).

The augmented specimens were tested within 60 days after augmentation. When not in use, the specimens were stored at -28°C and sealed in plastic bags. Under these conditions the resorbable phase of Calcemex-Spine remains unmodified. In fact, this investigation aimed at replicating the post-operative conditions.

In addition, four vertebrae from those spines were tested in the natural condition (Natural-1, Natural-2, Natural-3 and Natural-4): three of these specimens were part of a different study (Tozzi et al., in press 2016). These specimens are included in the present paper for comparison, as a blank control; more details about the natural specimens can be found in (Tozzi et al., in press 2016).

Within each spine segment, two vertebrae were assigned for augmentation with two types of bone cement, and one vertebra was used as the non-augmented control. Sampling was arranged so that the augmented and control samples were well distributed within the spine segment, in order to have at least one T1, one T2 and one T3 per group.

The growth plates were removed from the augmented and natural vertebrae, together with the adjacent endplates (due to the young age of the animals, this could be performed with little manual effort), similar to (Hardisty et al., 2010; Tozzi et al., in press 2016; Tozzi et al., 2015). A reproducible reference frame was adapted (Danesi et al., 2014), and the ends of each vertebra were potted in PMMA so that the cranio-caudal axis was consistently aligned with the loading direction within the micro-CT scanner (Fig.1). The neural arches were subsequently excised through resection of the pedicles.

2.2 Compression testing and micro-CT scanning

The augmented vertebrae underwent the same test protocol as the previous natural specimens (Tozzi et al., in press 2016).

Destructive tests were carried out under axial-compression with a customized-micro-mechanical loading device (CT5000, Deben Ltd, UK), equipped with a 5kN load cell and environmental chamber filled with 0.9% saline solution (Fig.1). To avoid translation and rotation of the specimens inside the chamber, a sandpaper disc was applied to the bottom loading platen. The force and displacement signals were acquired at 2Hz (Microtest-V6-2.67, Deben Ltd, UK).

A preload of 50 N was applied. Each specimen was subsequently compressed in displacement control, in a step-wise fashion (Fig.1). At each step, the actuator moved by 5% of the specimen's free height (this corresponded to actuator steps ranging between 0.47 and 0.67 mm, depending on the specimen). It must be noted that such actuator displacement included the actual bone compression, but also the compression of the PMMA pots, and the compliance of the entire loading system. The actuator speed was 0.1 mm/sec. At each step, the specimens were allowed to settle for 15 minutes, to reach a steady state prior to scanning. Most of the relaxation (Fig. 2-3) occurred during such 15 minutes. Some additional relaxation was unavoidable during imaging, but was one order of magnitude smaller than the initial one (it never exceeded 10% of the initial force).

Micro-CT imaging (XTH225, Nikon Metrology, UK) was carried out at each step (0% with 50N preload, 5%, 10% and 15% compression, Fig.1). The micro-CT scanner was set to a voltage of 88-89kV, a current of 110-116microA and exposure time of 2 seconds. Images were collected at rotational steps of 0.23° over 360°, for a scanning time of approximately 90

minutes at each compression step. The reconstructed micro-CT images had an isotropic voxel size of 38.8 micrometers.

2.3 Digital volume correlation (DVC)

The original micro-CT images were masked in correspondence to the contour, as regions with no pattern (e.g. saline solution) are associated with large correlation artifacts (Tozzi et al., 2015).

DaVis DVC software (v8.3, LaVision, Germany) was used to investigate the full-field strains. Briefly, DVC discretizes the 3D volume into sub-volumes, which are represented as a discrete grey-level function (Freddi et al., 2015). To correlate the patterns in the undeformed and deformed sub-volumes, a correlation function is applied. DaVis software deploys a multi-pass approach that uses the displacements from the previous pass to deform the sub-volume on the subsequent pass, until the highest possible correlation is achieved (Madi et al., 2013). In this application, a final sub-volume of 48 voxels (0% overlapping) was used, which was reached through passes of 128, 112, 96, 80 and 64 voxels. This multi-pass sequence was found to produce the lowest strain error for such types of specimens and imaging settings (Tozzi et al., 2015). The displacement and strain fields were calculated for each compression step (i.e. matching subsequent images: 0%-5%; 5%-10%, 10%-15%). The steps were then summed in a Lagrangian coordinate system.

A Matlab (v2014a, MathWorks, US) script was developed to visualize the 2D strain maps in sagittal and frontal planes. Moreover, for each compression step, the average strain within each transverse slice was computed for the axial, antero-posterior and lateral-lateral components of strain (Palanca et al., 2016).

3. RESULTS

3.1 Force-displacement curves

An initial toe region could be observed in the force-displacement curves (Fig. 2-3). Its extension was mainly dependent on the initial lack of co-planarity of the two pots.

For all the augmented specimens (Mendec-Spine, Fig. 2; Calcemex-Spine Fig. 3) the force increased monotonically as compression was applied, until failure. Relaxation was also visible at the end of each compression step, when the actuator was stopped to allow micro-CT

imaging. Failure in most cases was clearly detectable as the point where force reached a plateau or dropped. This occurred either during the third step (from 10% to 15% compression: specimens Mendec-2 and Calcemex-1), or during the second step (from 5% to 10% compression: all other specimens. The force at 15% compression was on average lower than the force at 10% compression (Table 1), confirming that the overall failure occurred before the end of the test. Inter-specimen variability never exceeded 35%; variability was larger at 5% compression, compared to 10% and 15% compression.

Some augmented specimens (Mendec-1, Mendec-3, Calcemex-1, Calcemex-2) were stronger than the respective controls (Tozzi et al., in press 2016), while others were weaker (Table 2).

3.2 Qualitative inspection of micro-CT images: internal damage

In all of the augmented specimens, the micro-CT images (Fig. 4-5) showed a main micro-damage, which started to be visible at the 10% compressive step, and degenerated into a trabecular collapse at 15%. For both cement types, the cement region appeared to be undamaged, even at the final loading stage (15% compression), where failure tended to initiate in the trabecular bone adjacent to the cement-bone interdigitated region.

In the majority of the Mendec-Spine specimens (3 out of 4, Fig. 4) the main micro-damage was localized in the trabecular bone at the mid-height and at the same level of the cement mass. Such a collapse seemed to initiate from the cement-bone interface, then gradually spread across the trabecular bone anteriorly and finally reaching the cortical bone in the transverse plane. In addition, Mendec-1 showed additional micro-damage just below the cement region (Fig. 4, 15% compression). Only for specimen Mendec-4 was collapse initiated at the two extremities (Fig. 4, 15% compression), which ended with a trabecular crushing in most of the cranial and caudal regions, far away from the augmented region.

The specimens augmented with Calcemex-Spine showed a main micro-damage localized in the trabecular region just cranial or caudal to the cement mass (Fig. 5, 15% compression). Only in Calcemex-2 the micro-damage was at the same height of the cement mass, towards the anterior of the specimen (Fig. 5, 15% compression). Similarly to the Mendec-Spine specimens, such a collapse initiated from the cement-bone interface, and gradually developed across the trabecular bone anteriorly or posteriorly in the transverse plane, in some cases affecting the cortical bone (Calcemex-1 and Calcemex-2).

In comparison with the control vertebrae (Tozzi et al., in press 2016) where failure initiated unpredictably in different regions of the natural vertebral body, failure in the augmented ones predictably initiated in the trabeculae adjacent to the cement mass.

3.3 Internal strain distribution: elastic regime and failure

As expected, the largest component of strain was the axial one, which was compressive (Fig. 6-7). The anterior-posterior and lateral-lateral components of strain (Supplementary Material) were smaller in magnitude, and mainly tensile (Poisson effect).

At the first compression step (5%) axial strains did not exceed -14000 microstrain, and localization of high-strain regions varied between specimens. Conversely, in the final loading step (15%) the cement regions seemed to be less strained in all specimens, and the largest strains were generally observed adjacent to the cement-bone interdigitated region.

In the Mendec-Spine specimens, the highest strains observed at 10% and 15% compression (sometimes close to 90000 microstrain) were at the mid-height and at the same level of the cement mass (Fig. 6). Conversely, in the Calcemex-Spine specimens the largest strains (50-60000 microstrain in most specimens; up to 110000 microstrain in Calcemex-2) were just cranial and caudal of the cement mass (Fig. 7). The highest strain was localized in a single region within the augmented vertebral body for most specimens; the only exceptions were Mendec-1 and Calcemex-4, where two distinct strain peaks were observed, adjacent to the cement mass. For the specimens augmented with both cement types, the regions of high strain (all components) seemed to match very well the localization of micro-damage visualized in the micro-CT images (Fig. 4-5). Strains were markedly lower away from the most stressed regions where damage initiated.

In comparison with the natural control vertebrae (Tozzi et al., in press 2016) the measured strain had the same order of magnitude. However, in the control vertebrae, the highest strain would unpredictably appear at any location inside the natural vertebral body.

The strain distribution in the augmented vertebrae in the elastic regime (5% compression) seemed to predict the location of the micro-damage initiation before it actually became identifiable (at 10% and 15% compression) in most of the specimens (Fig. 6-7). Only the specimen Mendec-2 showed a relocation of the highest axial strain from the posterior (5% compression, Fig. 6) to the anterior region (15% compression).

When the average axial strain was considered for each cross-section (Fig. 8-9), it was possible to observe how the strain progressively increased for different steps of compression: while at 5% compression no section was, on average, more strained than the others, at 10% and 15% it became possible to detect which sections of each vertebra was more strained. The strain pattern along the caudal-cranial direction was mostly similar among the Mendec-Spine specimens, with the largest deformation localized in correspondence of the specimen mid-height, or slightly displaced cranially as for Mendec-3 (Fig. 8). At 10% compression the average axial strain in the most strained cross-sections were 3-5 times higher than in the less strained ones; such differences became even more pronounced at 15% compression. The trend found for the four Mendec-Spine specimens was different from the natural controls (Tozzi et al., in press 2016), where the largest deformation was observed in correspondence of the cranial or caudal extremities. The strain pattern along the caudal-cranial direction of the four Calcemex-Spine specimens was different from the four Mendec-Spine specimens, but more similar to the natural controls (Tozzi et al., in press 2016) (Fig. 9).

4. DISCUSSION

The aim of this study was, for the first time, to measure the full-field internal strain distribution (all components of normal strain) by means of DVC in prophylactically-augmented vertebral bodies under compression. Specifically, we aimed to investigate the strain localization in the different regions of the augmented vertebral body (fully-augmented regions; cement-bone interdigitated regions; non-augmented bone tissue) with two different cements. We addressed both the strain distribution in the elastic regime, and failure initiation and propagation.

At a macroscopic level, similar forces were observed for the two types of cement. Our findings showed that augmentation increased the force required to induce damage in some of the vertebrae, compared to the natural controls. However, other augmented specimens (with both cement types) had a failure force lower than the natural controls. These findings were consistent with previous studies, which reported cases where prophylactically-augmented vertebrae were weaker than the untreated controls (Berlemann et al., 2002; Cristofolini et al., 2016; Dean et al., 2000). This inter-specimen variability in the weakening/strengthening effect (Table 2, Fig. 2-3) seems to confirm recent studies (Cristofolini et al., 2016; Widmer Soyka et al., 2016), in which it has been hypothesized that the effect of augmentation depends

on the quality of augmentation itself (i.e. amount, localization and distribution of the injected material).

Therefore, this study confirms the usefulness of DVC to investigate the internal strain distribution of augmented vertebrae, from the elastic regime up to failure. In fact, though a number of studies have used DVC to investigate the internal strain distribution of natural vertebrae under compression (Hardisty et al., 2012; Hussein et al., 2012; Hussein et al., 2013; Tozzi et al., in press 2016), the internal strain distribution of augmented vertebrae is still unexplored.

The results in this study clearly showed that prophylactic augmentation was not associated to an evident modification of the strain magnitude when compared to the control vertebrae, but rather to a different localization of the most strained regions, due to the cement distribution. Both the micro-CT images, and the DVC strain analysis highlighted that:

1. The cement mass was less strained than any other regions in the vertebra and never acted as strain concentrator for failure initiation. This can be explained by the additional stiffening and reinforcement associated with the infiltration of the cement inside the trabecular bone.
2. The highest strains and failure were localized in the bone adjacent to the cement-bone interdigitated region. This can be explained by the strain concentration between two regions: the cement-interdigitated bone, which has become stiffer and stronger, and the adjacent non-augmented trabecular bone (where some trabeculae might also have been damaged by the injection process).
3. The strain maps in the elastic regime and the localization of failure was different in the augmented vertebrae, when compared to the natural controls. This suggests an alteration of the load sharing in the augmented structure where the load is mostly carried by the cement region, rather than the trabecular core in the vertebra.
4. The specimens augmented with the two cement types seemed to have different failure mechanisms. Both failure (Fig. 4) and the highest strains (Fig. 6) with Mendec-Spine were mainly localized at mid-height, and at the same level of the cement mass. With Calcemex-Spine, both failure (Fig. 5) and the highest strains (Fig. 7) were mainly cranial and caudal to the cement mass. To confirm such findings, a larger sample size would be required.

The micro-CT images (Fig. 4-5) and the detailed DVC-computed strain maps (Fig. 6-7) allowed identification of the most strained region (even when localized in small volumes), already from the lowest degree of compression (5%). Conversely, the average strain in each cross-section (Fig. 8-9) allowed identification of the general trends, but not the single regions of high strain, which are predictors of failure.

It must be noted that when a given displacement was assigned to the actuator (i.e. the travel corresponding to 5% of the vertebral free height), this resulted in actual bone compression, but also compression of the PMMA pots, and small deformations of the entire loading system. Therefore, it is not possible to compare exactly the DVC-computed average compressive strains with the theoretical value of the compression steps (5%, 10%, 15%).

In summary: the most critical region was found at the boundary of the cement-bone interdigitated region, where the onset of the fracture was recognizable, consistently with previous studies (Tozzi et al., 2012, 2014). Starting from the cement-bone interdigitated region, the micro-damage gradually spread across the trabecular bone, which provided a lower stiffness than the injected cement. In most of the cases, the micro-damage in the trabecular bone was visible as compaction of the trabeculae, which is associated with bending and buckling of trabeculae in the transverse plane (Tozzi et al., 2012).

It is known that augmentation in some cases weakens the vertebra compared to the untreated one (Berlemann et al., 2002; Dean et al., 2000). A recent study based on destructive testing and surface strain measurement (Cristofolini et al., 2016) suggested that such a weakening might be associated with the interaction of the cement mass with the host bone, if augmentation is sub-optimal. It has been shown (Cristofolini et al., 2016; Kinzl et al., 2012) that weakening tends to occur when the cement mass is far from the endplates, whereas augmentation strengthens the vertebra when a cement bridge is formed between the endplates. Our DVC investigation demonstrated, for the first time, that augmentation reinforces the regions where cement is actually delivered (reduced strain), but localizes higher strains at the boundary of the cement-interdigitated bone. If such a strain concentration occurs where the bone is strong (i.e. close to the endplates) this may not result in a critical weakening; conversely, if it occurs where the trabecular bone is weaker, this may facilitate failure.

The perturbation of the internal strain distribution observed with the present DVC study could explain the clinically-reported fracture in the vertebrae adjacent to the augmented one (Grados et al., 2000; Han et al., 2009; Kim et al., 2004; Trout et al., 2006; Uppin et al., 2003).

There are some limitations in this study that must be considered. First of all, porcine specimens were used, which have a different anatomy and tissue properties than human tissues (Brandolini et al., 2014). The vertebral body heights of porcine T1 and T2 are equivalent to those of the human T1 and T2, while T3 is taller than the human T3; the endplate areas of porcine T1, T2 and T3 are 36%-53% smaller than the humans (Bozkus et al., 2005). In the current study it was necessary to use porcine specimens, because of the limited dimension and space available for the loading device inside the micro-CT-scanner. The bone mineral density of the porcine vertebrae is higher when compared to the human vertebrae (Aeressens et al., 1998). For this reason the amount of cement that could be injected in our specimens was significantly lower than the typical amount injected in humans. Furthermore, despite their smaller size, the strength of the porcine vertebrae was of the same order of magnitude as the human ones. For this reason, the current results cannot be entirely indicative from a clinical perspective, as both the failure force and the strain magnitude may differ from human vertebrae. However, comparisons between natural and augmented specimens, and between different types of cement are possible. Furthermore, this study allowed, for the first time, a complete *in vitro* characterization of the internal failure mechanism in the augmented vertebral body.

Another limitation is the relatively small sample size: 4 specimens were tested for each group, preventing any conclusive statistical comparisons. Larger samples (n=30-66) were tested when only the failure force was measured (Furtado et al., 2007; Heini et al., 2001; Lim et al., 2002). As in our study, where we investigated in detail the internal strain distribution, a smaller number of specimens could be considered.

The inter-specimen differences in failure mechanism observed (e.g. Mendec-4 differed from the other Mendec-Spine specimens) could either be caused by the different localization of the cement mass (which unavoidably occurs as the cement flows inside the bone) or by sub-optimal alignment of the pots at the extremities.

All these limitations are compensated by the fact that, to the author's knowledge, this is the first time that the internal strain distribution (from elastic to post yield regime) through DVC

398 was employed to investigate the internal failure mechanism in prophylactic-augmented
399 vertebrae.

400 **5. CONCLUSIONS**

401 In conclusion, this study has demonstrated the potential of digital volume correlation in
402 measuring the internal strain and failure in prophylactically-augmented vertebrae. It has been
403 shown that failure starts inside the augmented vertebral body, next to the injected cement
404 mass. This information (in terms of localization of the cement mass) can help improve
405 treatment protocols for vertebroplasty.

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CAPTIONS

Fig. 1 - Overview of the experimental design. The vertebral bodies were dissected from the spine segments, removing all soft tissues. Prophylactic augmentation was performed on the selected specimens with two types of cements (Mendec-Spine and Calcemex-Spine). The remaining specimens were used as untreated controls as part of a different study (Tozzi et al., in press 2016). The ends of each vertebra were potted in PMMA. Destructive tests were carried out under axial-compression in a step-wise fashion. Micro-CT imaging was acquired at each loading step (0% with 50 N preload, 5%, 10% and 15% compression). Finally, digital volume correlation (DVC) was performed to compute the internal full-field strains.

Fig. 2 - Force-compression curves for the four specimens augmented with Mendec-Spine. The force showed a drop at the end of each step of compression: this corresponded to the stress relaxation while the specimen was allowed to settle (15 minutes), before the micro-CT scan took place (90 minutes).

Fig. 3 - Force-compression curves for the four specimens augmented with Calcemex-Spine. The force showed a drop at the end of each step of compression: this corresponded to stress relaxation while the specimen was allowed to settle (15 minutes), before the micro-CT scan took place (90 minutes).

Fig. 4 - Specimens augmented with Mendec-Spine: sagittal micro-CT slice at each compression step (“A” indicates anterior, “P” posterior). Micro-damage started to be visible at 10% compression; at the last step (15% compression) damage became fully visible (red arrows). Conversely, no micro-damage could be observed in any specimen at the first step (5% compression).

Fig. 5 - Specimens augmented with Calcemex-Spine: sagittal micro-CT slice at each compression step (“A” indicates anterior, “P” posterior). Micro-damage started to be visible at 10% compression; at the last step (15% compression) damage became fully visible (red arrows). Conversely, no micro-damage could be observed in any specimen at the first step (5% compression).

Fig. 6 - Specimens augmented with Mendec-Spine: Internal strain distribution for the three steps of compression. The axial component of strain (in microstrain) is shown for the 4 specimens over the same sagittal slice as in Fig. 4 (the antero-posterior and lateral-lateral components of strain are reported in the Supplementary Material). The most strained regions corresponded to the damaged region, which gradually progressed into a collapse propagating across the trabecular bone.

Fig. 7 - Specimens augmented with Calcemex-Spine: Internal strain distribution for the three steps of compression. The axial component of strain (in microstrain) is shown for the 4 specimens over the same sagittal slice as in Fig. 5 (the antero-posterior and lateral-lateral components of strain are reported in the Supplementary Material). The most strained regions corresponded to the damaged region, which gradually progressed into a collapse propagating across the trabecular bone.

Fig. 8 - Specimens augmented with Mendec-Spine: Progression of strain with compression steps (5%, 10% and 15%). The average strain (in microstrain) was computed for each transverse slice for the axial component of the DVC-computed strain maps. In general, an incremental strain pattern among the consecutive compression steps was observed in all specimens. The slices where the largest strains were observed corresponded to the regions where internal damage was localized in the vertebra (Fig. 4 and 6).

Fig. 9 - Specimens augmented with Calcemex-Spine: Progression of strain with compression steps (5%, 10% and 15%). The average strain (in microstrain) was computed for each transverse slice for the axial component of the DVC-computed strain maps. In general, an incremental strain pattern among the consecutive compression steps was observed in all specimens. The slices where the largest strains were observed corresponded to the regions where internal damage was localized in the vertebra (Fig. 5 and 7).

TABLES

Table 1: Force experienced by the eight augmented specimens at each step of compression (absolute value). Average, standard deviation and coefficient of variation are indicated for both groups.

Augmented Specimens	Force at 5% compression	Force at 10% compression	Force at 15% compression
Mendec-1	3058 N	3222 N	3403 N
Mendec-2	1502 N	4125 N	4064 N
Mendec-3	3089 N	4481 N	4036 N
Mendec-4	2532 N	4267 N	4053 N
Mendec: Average (SD)	2545 N (741 N)	4024 N (554 N)	3889 N (324 N)
Mendec: Coefficient of variation	29%	14%	8%
Calcemex-1	1101 N	3007 N	2057 N
Calcemex-2	2088 N	4527 N	3802 N
Calcemex-3	1388 N	2762 N	2463 N
Calcemex-4	2345 N	3423 N	3408 N
Calcemex: Average (SD)	1731 N (583 N)	3430 N (781 N)	2933 N (810 N)
Calcemex: Coefficient of variation	34%	23%	28%

Table 2: Force experienced by the eight augmented specimens at each step of compression as a fraction of the force in the corresponding natural control vertebra (a value greater than 1.00 indicates that the augmented vertebra experienced a larger force than the control). Average, standard deviation and coefficient of variation are indicated for both groups.

Augmented Specimens	Force at 5% compression (fraction of natural control)	Force at 10% compression (fraction of natural control)	Force at 15% compression (fraction of natural control)
Mendec-1	2.74	1.53	1.55
Mendec-2	1.47	1.00	1.02
Mendec-3	1.06	1.25	1.07
Mendec-4	0.83	Missing data for the control	
Mendec: Average (SD)	1.52 (0.85)	1.26 (0.26)	1.21 (0.29)
Mendec: Coefficient of variation	56%	21%	24%
Calcemex-1	0.99	1.43	0.94
Calcemex-2	2.04	1.10	0.95
Calcemex-3	0.48	0.77	0.65
Calcemex-4	0.77	Missing data for the control	
Calcemex: Average (SD)	1.07 (0.68)	0.88 (0.33)	0.85 (0.17)
Calcemex: Coefficient of variation	64%	37%	20%

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