Medical Engineering and Physics 65 (2019) 46–56

Contents lists available at ScienceDirect

Medical Engineering and Physics

journal homepage: www.elsevier.com/locate/medengphy

Prophylactic vertebroplasty versus kyphoplasty in osteoporosis: A comprehensive biomechanical matched-pair study by in vitro compressive testing

Marta Kurutz[a,*], Peter Varga[b], Gabor Jakab[c]

[a] Budapest University of Technology and Economics, Műegyetem rkp. 3, H-1111 Budapest, Hungary
[b] AO Research Institute Davos, Clavadelerstrasse 8, 7270 Davos Platz, Switzerland
[c] National Center for Spinal Disorders, Királyhágó u. 1, H-1126 Budapest, Hungary

A R T I C L E I N F O

Article history:
Received 19 October 2018
Revised 15 January 2019
Accepted 24 January 2019

Keywords:
Vertebroplasty
Kyphoplasty
Prophylactic augmentation
Biomechanical testing
Cement-endplate contacts

A B S T R A C T

Vertebroplasty and kyphoplasty are alternative augmentation techniques of osteoporotic vertebral compression fractures. However, shortly after augmentation, new vertebral compression fractures may occur, mostly in the adjacent vertebrae. To prevent this, prophylactic cement injection can be applied to the neighboring vertebral bodies. Although there are many evidence-based clinical studies on the potential hazards of vertebroplasty and kyphoplasty, there are only few studies comparing the prophylactic potential of the two treatments. In this matched-pair experimental biomechanical study, the two treatments were compared via destructive compressive testing of 76 non-fractured osteoporotic human lumbar vertebral bodies from 24 cadavers, augmented pair-wise with vertebroplasty or kyphoplasty. Strength, stiffness and deformability were analyzed in terms of donor age, CT-based bone density, vertebral morphometry, and cement-endplate contacts. These were investigated in a paired analysis and also in terms of the number of cement-endplate contacts. Vertebroplasty resulted in significantly, but only 19% larger stiffness, approximately equal failure load and smaller failure displacement compared to kyphoplasty. Cement-endplate contacts affect augmentation differently for the two techniques, namely, strength significantly increased with increasing number of contacts in vertebroplasty, but decreased in kyphoplasty. The reasons for these contrasting behavior included the fundamentally different augmentation method, the resulting different construction and location of cement clouds and the different form and location of failure. These results indicate that both prophylactic vertebroplasty and kyphoplasty of non-fractured adjacent vertebrae may be advantageous to avoid subsequent fractures after post-fracture vertebroplasty and kyphoplasty, respectively. However, cement bridging in vertebroplasty and central cement placement in kyphoplasty are advantageous in prevention.

1. Introduction

Osteoporotic vertebral compression fractures (VCF) belong to the most frequent morbidities related to the spine, causing instability, deformity, pain and deteriorated quality of life [1,2]. Two minimally invasive techniques, vertebroplasty (VP) and kyphoplasty (KP) were developed for the treatment of these injuries. In VP, bone cement is injected percutaneously in trans- or peripedicular, uni- or bilateral way into the fractured vertebral [3–8]. However, VP is limited by the potential leakage of cement and it cannot restore the vertebral height [9–11]. Therefore, in KP, one or two balloon tamps are first inserted into the vertebral body and inflated to prepare place for the cement before filling and to expand vertebral height [12–14]. Both treatments restore strength and stiffness of fractured vertebrae and provide clinical benefits [15–17]. However, shortly after both treatments, new VCFs can develop in the vicinity of the intervention, mostly in adjacent vertebrae (AVF). The incidence of subsequent fracture shows considerable variation across studies with reported values ranging from 8–52% following VP and from 3–29% following KP [18–27]. Reported risk factors included higher age, intravertebral clefts, thoracolumbar junction and shorter distance to the treated vertebrae in VP; greater degree of height restoration of the cemented vertebrae in KP; and low bone mineral density in both treatments [28–30]. The large variations in the incidences of AVFs suggest that prevention is equivalently important for both approaches.

Despite the frequent occurrence of postsurgical fractures, very few studies have investigated prophylactic augmentation.

* Corresponding author.
E-mail addresses: kurutzm@eik.bme.hu (M. Kurutz), peter.varga@aofoundation.org (P. Varga), gabor.jakab@bhc.hu (G. Jakab).

https://doi.org/10.1016/j.medengphy.2019.01.004
1350-4533/

Kobayashi et al. [31] performed prophylactic VP in the non-fractured vertebra superior to the post-fracture augmented vertebra of 155 patients, with no prophylactic VP in a control group of 89 patients. The three-months incidence of new, mainly adjacent vertebral fractures was 4.5% and 16.8%, and the one-year incidence was 9.7% and 22.4% in the prophylactic and control groups, respectively. To find the new VCF risk of multiple fractures, Kamano et al. [32] monitored 116 patients with adjacent prophylactic VP above multiple fractured vertebral segments. They concluded that three or more preoperative fractures provoke subsequent fractures even with prophylactic VP, but there was no increased risk of subsequent fractures related to prophylactic VP. Becker et al. [33] found a refracture rate of 22% in 30 post-fracture KP patients and 26% in 30 post-fracture KP with prophylactic KP, concluding that there was no indication for prophylactic kyphoplasty. Eichler et al. [34] compared 19 post-fracture KP and 18 post-fracture KP with simultaneous prophylactic VP. At a mean follow-up of 16 months, they found AVF in 50% of the prophylactic and 16% in the KP group, concluding that prophylactic VP after KP does not decrease the refracture risks.

Even fewer studies have investigated prophylactic augmentation biomechanically. Unipedicular prophylactic VP with 20% cement filling was shown by Higgins et al. [35] to increase the strength of non-fractured vertebrae by 36% on average, with a relatively larger improvement occurring in specimens with lower BMD. Sun and Liebschner [36] used computational modeling to investigate the effect of BMD on the biomechanical efficacy of cement augmentation. Their predictions suggested that augmentation was more effective for low trabecular densities, with a bipedicular injection of 20% volume fraction of PMMA being optimal for alleviating fracture risk. In turn, for vertebrae with densities above 0.22 g/cm^3, prophylactic vertebroplasty was not required. Osteoporotic non-fractured and pre-fractured vertebrae were tested under eccentric compression by Furtado et al. [37], concluding that prophylactic augmentation increased failure strength and maintained stiffness better than post-fracture VP. Fourteen 5-level thoracic segments divided into standard and prophylactic VP groups were tested cyclically by Chiang et al. [38], demonstrating that prophylactic augmentation strengthened the osteoporotic vertebrae to prevent AVF. Post-fracture and prophylactic VP was compared by Hulme et al. [39] on spinal segments under axial loading. They found that the deformation in the augmented endplate was significantly reduced for both prophylactic and fracture group. Aquarius et al. [40] compared three cadaveric models: unfilled vertebrae loaded axially, loaded 20° off-axis and filled with cement and loaded 20° off-axis, representing vertebrae in non-fractured spine, adjacent to a fracture and adjacent with prophylactic VP, respectively. Prophylactic augmentation resulted in 32% greater failure load and 27% higher stiffness than the unfilled adjacent group, and equal failure load and 21% lower stiffness than the non-fractured group, concluding that prophylactic VP can decrease the fracture risk.

These previous investigations showed that the occurrence of postsurgical fractures was almost an equally important problem for both VP and KP, consequently, the prevention is equally important task for both treatments.

To the authors' knowledge, a comprehensive experimental biomechanical comparative analysis of the prophylactic potential of the two alternative augmentation methods has not been performed so far. Therefore, the aim of this study was to fill this gap by investigating and directly comparing the strengthening effect of the two augmentation approaches in terms of prevention. We hypothesized that the two different methods of cement injection yielded different structure and location of cement clouds, leading to different strength and stiffness with different forms and locations of failure in the prophylactically augmented VP and KP vertebrae. A preliminary report has been published formerly on the results of a pilot study with a relatively small sample set [41].

2. Methods

Human cadaveric spines were obtained from the Patora Health Service Unit of Semmelweis University and prepared in the National Center for Spinal Disorders in Budapest, Hungary. All experiments were performed in the laboratory of the Biomechanical Research Centre of the Budapest University of Technology and Economics in line with the Hungarian legislative requirements.

2.1. Specimen preparation

Ninety-four non-fractured human vertebrae, 7 thoracic and 87 lumbar (1 T11, 6 T12, 17 L1, 21 L2, 22 L3, 18 L4 and 9 L5) were extracted from the spines of 24 human donors, 10 males with age range of 60–89 years (65.9 ± 9.5 years) and 14 females with age range of 51–95 years (72.9 ± 15.5 years). Both endplates of the vertebrae were embedded into polymethylmethacrylate (PMMA) resin with an approximate depth of 4.5 mm. The samples were divided into two groups by alternatively assigning adjacent vertebrae originating from the same donor and operated with either VP ($N = 48$) or KP ($N = 46$) (Fig. 1). The same amount of 3 + 3 ml PMMA cement was injected bipedicularly, following the standardized surgical protocol of the National Center for Spinal Disorders. For the adjacent pairs, the distribution of vertebroplasty and kyphoplasty was equal between the cranial and caudal vertebra of a vertebral pair.

2.2. CT scanning and evaluation

Each specimen was scanned with a high-resolution quantitative computed tomography (QCT) system (Hitachi Presto, Hitachi Medical Corporation, Tokyo, Japan) at three time points: before operation (pre-op), after operation (post-op, Fig. 1) and after the compressive test (post-test, Fig. 2). Scanning settings were 120 kVp energy, 150 mA current, 150 ms exposure time, 512 × 512 pixel matrix, 0.47 mm in-plane pixel size, 0.75 mm slice thickness. The bones were scanned submerged in a water-filled box to mimic the attenuation and scattering effects of soft tissues surrounding the spine in vivo. The Hounsfield unit voxel values (HU) were converted to bone mineral density units (BMD, in mg/cm^3) using a calibration law evaluated for each specimen individually based on the calibration phantom with five rods of different mineral densities [42,43]. Average volumetric BMD (vBMD) was quantified within three trabecular bone compartments (superior and inferior subcortical levels, located 1–3 mm from the cranial and caudal endplate, respectively; and central level at the smallest cross-sectional area) on the pre-op QCT images [44]. Vertebrae with vBMD values between 80 and 120 mg/cm^3 were defined to be osteopenic and below 80 mg/cm^3 to be osteoporotic [45–47].

Vertebral morphometry was measured on the pre-op CT scans, including superior, inferior and central cross sectional areas; coronal and sagittal peripheral and central heights; coronal and sagittal superior, inferior and central widths. Volume of vertebrae was calculated from these measures. All geometric parameters were measured and evaluated after the compressive tests, too. All CT scans were analyzed by a single person and the same criteria were used for all samples.

Regional areas and heights of cement, superior and inferior distances between cement clouds and endplates were measured on the post-op CT scans. The following parameters were defined and quantified in percent: cement volume fraction (CVF) as the ratio of cement and vertebral volumes; cement area fraction (CAF) being the ratio of maximum cement area in any CT slice and the vertebral cross sectional area in the same slice; cement height fraction

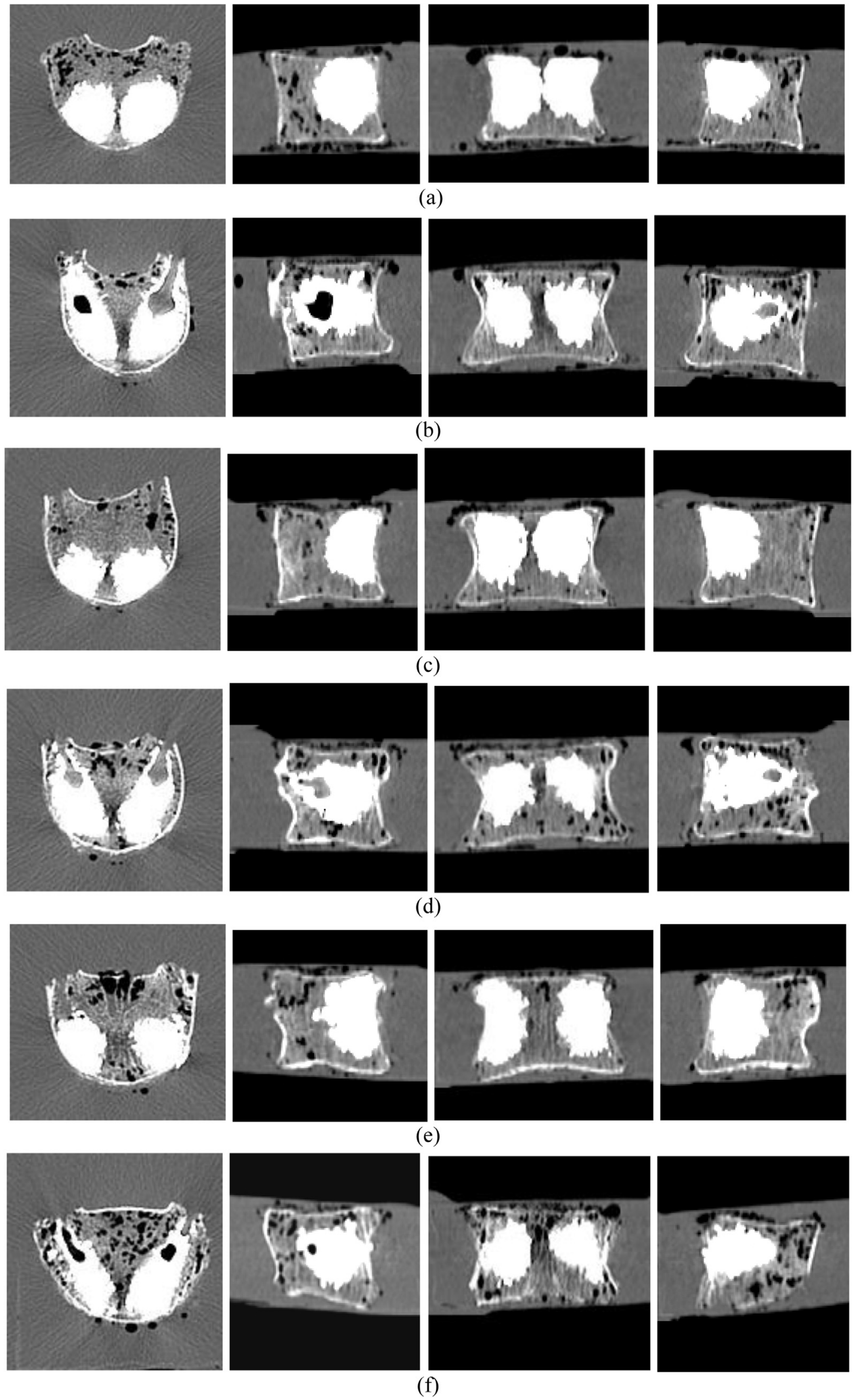

Fig. 1. Series of transverse, left sagittal, coronal and right sagittal (from left to right) post-op CT slices of the lumbar spinal vertebrae of a 58 years old man. (a) T12, VP; (b) L1, KP; (c) L2, VP; (d) L3, KP; (e) L4, VP; (f) L5, KP. T refers to thoracic, L to lumbar, VP to vertebroplasty and KP to kyphoplasty.

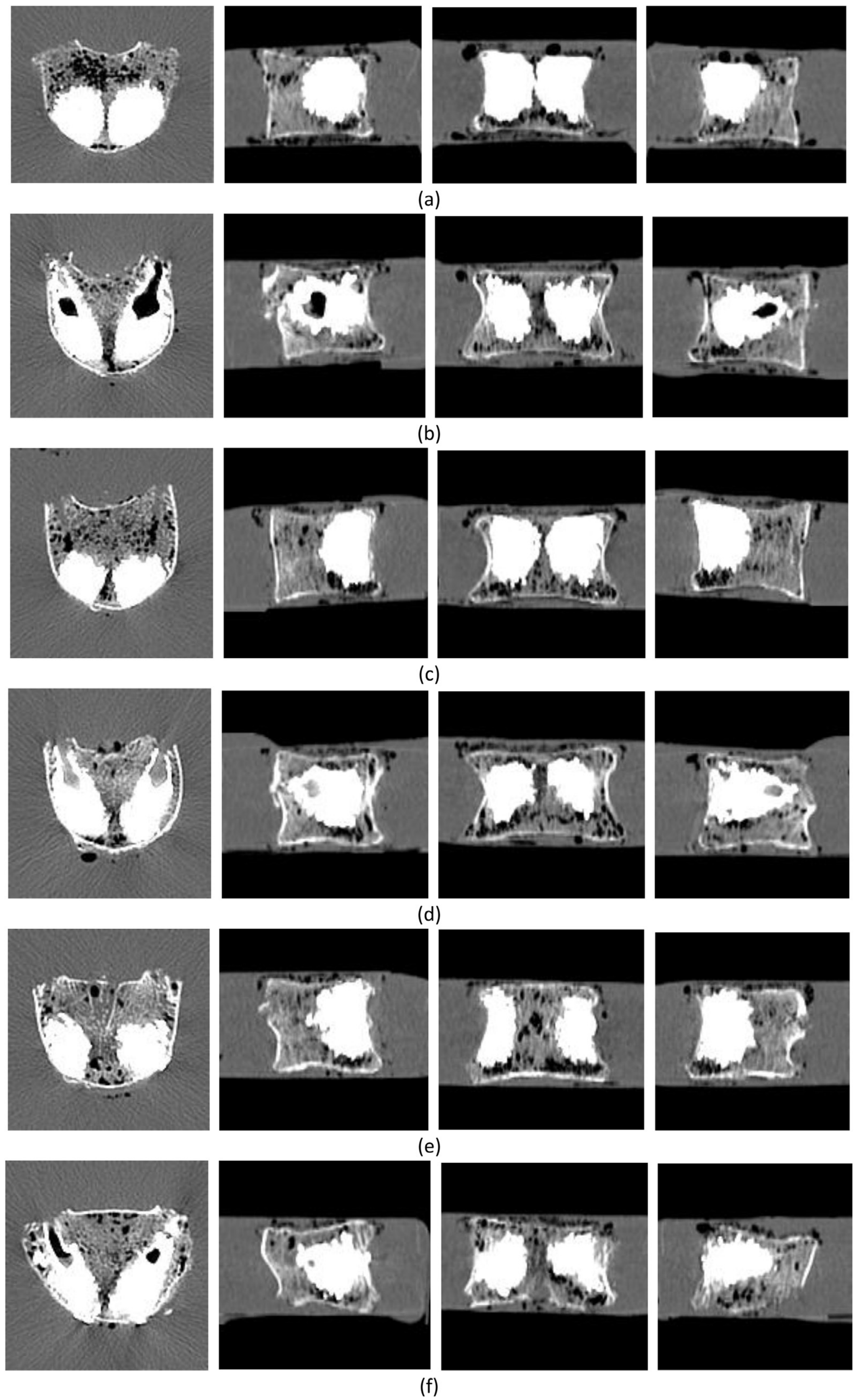

Fig. 2. CT slices after the compression test of the same lumbar spine segments shown in Fig. 1. Series of transverse, left sagittal, coronal and right sagittal (from left to right) sections: (a) T12, VP; (b) L1, KP; (c) L2, VP; (d) L3, KP; (e) L4, VP; (f) L5, KP. T refers to thoracic, L to lumbar, VP to vertebroplasty and KP to kyphoplasty.

(CHF) as the ratio of the average height of the two cement clouds and the average vertebral height; and the total, superior and inferior cement-free distance fractions (CDF). The superior and inferior CFDs were measured for both the left and the right cement clouds and averaged. The total CDF was the sum of the superior and inferior CDFs. Based on the difference of the measurements on post-op and post-test CT scans, the plastic displacements were determined.

Contact was defined if the cement cloud reached one of the two endplates on post-op CT scans. Considering the two separate cement clouds in a vertebra, five cases of possible contacts were defined: no-contact, one-, two-, three- or four-contacts. A cement bridge formed if a cloud contacted both endplates. Each vertebra was classified into the corresponding contact group.

The form and extent of failure in the trabecular bone were identified based on the comparison of post-op and post-test CT scans (Figs. 1 and 2). Failure was defined as the dark regions appearing after testing.

2.3. Mechanical testing and evaluation

The specimens were stored at −20 °C following CT scanning and were thawed at room temperature 4–6 h before testing. Destructive mechanical testing was performed by applying uniaxial displacement-driven compressive loading on the outer surfaces of the embedding layers by means of parallel metal plates mounted to a servohydraulic testing device (Instron 8872 series, Instron, Norwood, USA). Loading rate was set to 5 mm/min to ensure quasi-static conditions, the displacement of the cross-head and the force in the load cell were recorded. The full scale of the load cell was 25 kN (Instron Dynacell 2527). The test was stopped either at 20% reduction in the resisting force or at 20% total deformation.

From the 94 operated vertebrae, 10 specimens (6 VP and 4 KP) were excluded due to *a priori* fractures observed on the CT images; no measurable load bearing capacity and unusable load-displacement curves; or excessive strength causing forces which could not be measured due to the limitation of the load cell. Moreover, 8 specimens (4 KP and 4 VP) were excluded due to more than 20% cement leakage, leaving 38 adjacent pairs (17 males and 21 females) for further analyses.

The first peak of the force-displacement curves (Fig. 3a–d) defined failure load and displacement (Fig. 3e). Elastic stiffness was the slope of the linear portion. Proportional load and displacement were defined by the end of the linear part. Maximum displacement was indicated by the point where the loading process stopped. Post-failure displacement was the difference between the maximum and failure displacements. Failure strain was derived as the ratio of the failure displacement and the initial vertebral height.

The total energy at failure was the area under the load-displacement curve at failure. The corresponding recovered elastic energy was calculated by assuming classical elastic-plastic unloading process parallel to the stiffness line. The dissipated energy was the difference between the total and the recovered energies. Energy dissipation capacity was the ratio of the dissipated to the total energy.

2.4. Statistics

A matched-pair study design was applied to the adjacent pairs of VP and KP specimens [48,49]. Two-sided, paired student's *t*-test was used to calculate the *P*-value related to the standard error of the difference between the means of the properties. First, we tested the hypothesis that the two treatment groups were not different in terms of the donor and augmentation properties. Then, the null hypothesis was tested that there was no difference in the mechanical results between vertebrae treated with VP or KP. The Bonferroni correction was applied for multiple comparisons [50].

In the analysis based on the number of cement-endplate contacts, VP and KP could not be compared pair-wise. Therefore, VP and KP were analyzed separately in terms of their contact conditions, and the effects of contact cases on the mechanical behavior were compared.

Linear regression analysis was used to determine the correlation of the mechanical results with donor and augmentation features and contact cases. The degree of association was measured by Pearson's correlation coefficient (R) and the strength of the relation was tested for significance using the *t*-test. $P < 0.05$ was considered significant.

3. Results

3.1. Comparison between VP and KP specimens – paired analysis results

Donor age, vBMD, and vertebral morphometry measures were not significantly different between VP and KP (Table 1). Both in VP and KP, 50% of the samples was osteopenic and 26% was osteoporotic.

Cement areas and area fractions, cement-free distances to endplates and distance fractions were significantly larger, cement

Table 1
Donor characteristics, cement augmentation data, and embedment thickness for VP and KP treated specimens. Mean values with +/− SD are indicated. The stars (*) indicate the significance $P \le 0.05/20 = 0.0025$ for donor and $P \le 0.05/12 = 0.0042$ for augmentation data, by considering the simultaneous 20 comparisons for donor and 12 for augmentation and embedment data in Bonferroni correction applied separately for VP and KP groups. Notation *ns* means non-significance. The abbreviations are as follows: vBMD: volumetric bone mineral density, CVF: cement volume fraction, CAF: cement area fraction, CHF: cement height fraction, CDF: cement distance fraction.

Vertebral properties	VP	KP	P
Number of pairs	$n = 38$	$n = 38$	
Donor age	68.6 ± 12.9	68.6 ± 12.9	ns
Volumetric BMD (mg/cm^3)	102±27	103 ± 31	ns
Area (mm^2)			
Superior	1562 ± 345	1545 ± 370	ns
Inferior	1486 ± 285	1472 ± 308	ns
Central	1239 ± 284	1239 ± 275	ns
Height (mm)			
Sagittal anterior	28.4 ± 2.6	28.2 ± 2.8	ns
Sagittal posterior	28.6 ± 2.3	28.4 ± 2.2	ns
Sagittal central	25.4 ± 1.9	25.1 ± 2.0	ns
Mean sagittal	27.0 ± 1.9	26.7 ± 2.0	ns
Mean coronal peripheral	28.1 ± 2.2	28.1 ± 2.6	ns
Coronal central	25.7 ± 1.8	25.4 ± 2.1	ns
Mean coronal	26.9 ± 1.8	26.7±2,2	ns
Mean peripheral	28.3 ± 2.1	28.2 ± 2.4	ns
Mean central	25.5 ± 1.7	25.2 ± 2.0	ns
Mean total	26.9 ± 1.8	26.7 ± 2.1	ns
Width (mm)			
Coronal subcortical	51.3 ± 6.0	51.0 ± 6.0	ns
Coronal central	42.3 ± 6.0	42.5 ± 6.0	ns
Sagittal subcortical	35.5 ± 4.3	35.8 ± 4.3	ns
Sagittal central	32.4 ± 3.8	32.3 ± 3.7	ns
Volume (mm^3)	37,479±9563	37,072±10,043	ns
Cement			
Volume fraction, CVF (%)	17.0 ± 4.4	17.4 ± 5.0	ns
Maximum area (mm^2)	545 ± 74	711 ± 82	*
Maximum area fraction, CAF (%)	46 ± 12	60 ± 12	*
Maximum height (mm)	23.6 ± 2.4	19.9 ± 2.4	*
Maximum height fraction, CHF (%)	87.7 ± 8.0	75.1 ± 10.9	*
Distance to superior endplate (mm)	0.5 ± 0.9	1.6 ± 1.7	*
Distance to inferior endplate (mm)	2.9 ± 1.9	5.2 ± 2.4	*
Free distance sum (mm)	3.4 ± 2.2	6.8 ± 3.2	*
Free distance fraction, CDF (%)	12.3 ± 8.0	24.9 ± 10.9	*
Superior CDF (%)	1.8 ± 3.6	5.8 ± 5.9	*
Inferior CDF (%)	10.5 ± 6.9	19.0 ± 8.5	*
Embedment, mean thickness (mm)	4.69 ± 2.20	4.74 ± 2.28	ns

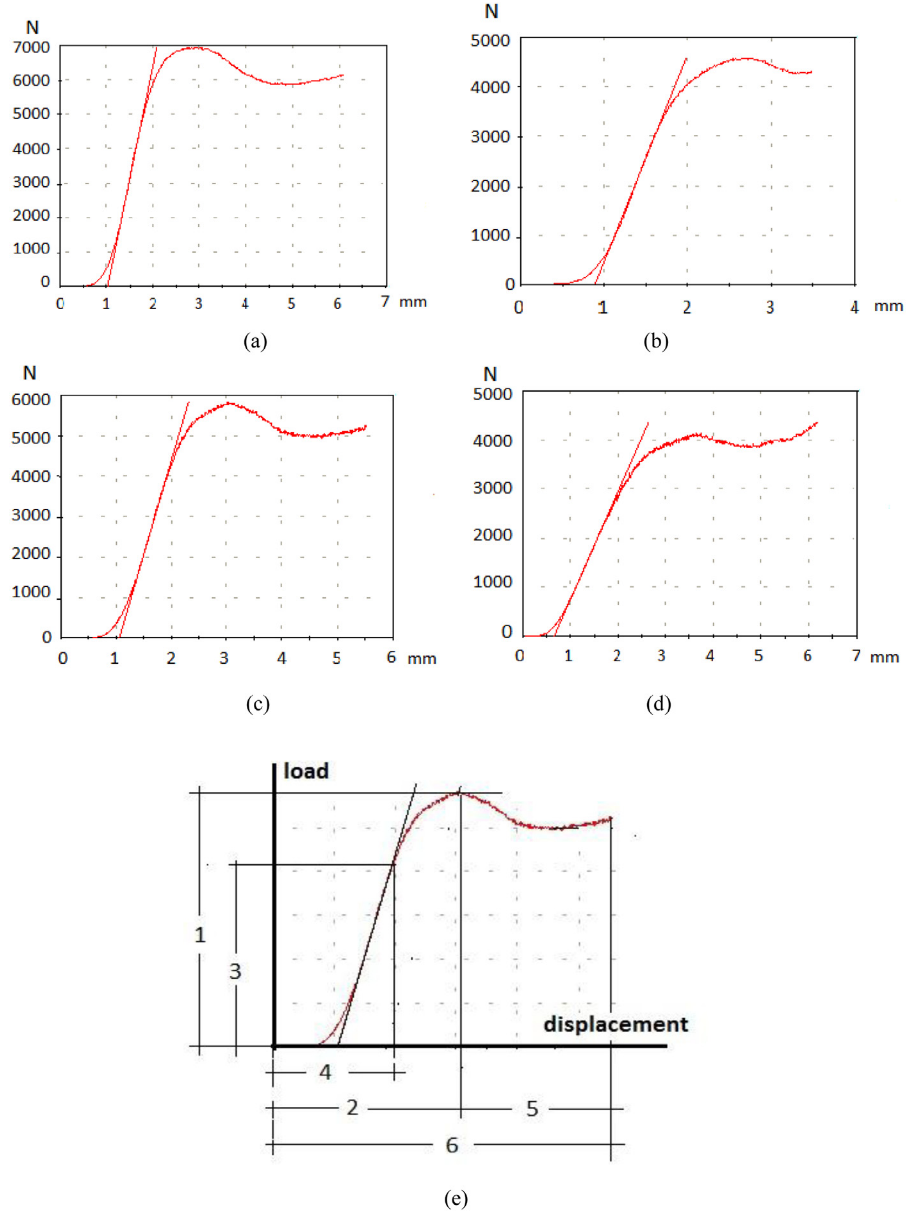

Fig. 3. Experimentally obtained load-displacement curves of compression load (N) and displacement (mm): (a) vertebroplasty (VP) male, (b) VP female, (c) kyphoplasty (KP) male and (d) KP female specimens. The parameters extracted from the curve are illustrated on a typical load-displacement curve in (e): 1 – failure load, 2 – failure displacement, 3 – proportional load, 4 – proportional displacement, 5 – postfailure displacement, 6 – maximum displacement.

heights and height fractions were significantly smaller in KP. Cement volume fraction and embedding thickness was not significantly different between the two groups.

Elastic stiffness was significantly larger in VP (by 19%), failure load and displacement were not significantly different between the two treatments, CT-based plastic displacement was significantly larger in VP (by 31%, Table 2). Energy dissipation capacity ratio at failure was equally 56% in both groups.

3.2. Correlation of mechanical results with donor and augmentation properties for VP and KP specimens

Failure load and stiffness had moderate positive correlation with vBMD, but only in KP (Table 3). In both treatment groups, failure load and stiffness showed moderate/strong positive correlation with vertebral areas, widths and volume; and negative correlations with CVF and CAF. Failure load and stiffness had positive correlation with maximum cement area, but only in KP group. Failure load and stiffness were strongly correlated.

In VP, failure displacement correlated positively with vertebral areas, widths and volume, but not with heights. In turn, in KP, it correlated mostly with vertebral heights (Table 3). Moreover, failure load and displacement correlated (positively) with maximum cement height in VP, but not in KP. Failure displacement correlated (positively) with vertebral height in KP, but not in VP. Failure load, failure displacement and stiffness in KP were correlated with vertebral height, but not with cement height.

3.3. Correlation of mechanical results with donor and augmentation properties for VP and KP – results of the contact groups

Cement-endplate contacts were observed in 92% of VP and 63% of KP specimens, across five and four contact groups, respectively (Table 4). Both in VP and KP, the two-contact cases occurred with

Table 2
Main mechanical results for VP and KP treated specimens, extracted from the load-displacement curves (see Fig. 3e) and from the CT scans (mean ± SD). The stars (*) indicate the significance $P \leq 0.05/10 = 0.005$ by considering 10 comparisons for data obtained from the load-displacement curves in Bonferroni correction, applied separately for VP and KP groups. For values obtained from CT scans $P \leq 0.05$ means significance. Abbreviation *ns* means non-significance.

Test results Number of pairs	VP $n = 38$	KP $n = 38$	P
From load-displacement curves			
Failure load (N)	5158 ± 1428	4925±1511	ns
Failure displacement (mm)	2.70 ± 0.79	3.04±0.70	ns
Failure strain (%)	10.0 ± 2.9	11.4 ± 2.4	ns
Elastic stiffness (N/mm)	4605 ± 1580	3863 ± 1314	*
Proportional load (N)	3635 ± 1115	3456 ± 1101	ns
Proportional displacement (mm)	1.61 ± 0.47	1.83 ± 0.46	ns
Postfailure displacement (mm)	2.35 ± 1.05	2.19 ± 0.92	ns
End displacement (mm)	5.05 ± 1.26	5.23 ± 096	ns
Recovered energy at failure (mJ)	3110 ± 1406	3284 ± 1316	ns
Absorbed energy at failure (mJ)	4023 ± 3093	4205 ± 3025	ns
From CT- scans			
Plastic displacement (mm)	1.48 ± 0.79	1.13 ± 0.46	*

the same endplate (mainly with the superior one), without bridging the endplates. There were two exceptions in VP and one in KP, where one of the clouds contacted the superior, the other cloud the inferior endplate, without forming any bridge. Both cement clouds contacted the anterior cortical wall nearly in all VP specimens (37 from 38), while only in half of the KP samples.

There was a monotonic increase of failure load with increasing number of cement-endplate contacts and decreasing CDF in VP, but in KP all these trends had opposite signs (Table 4). Failure load showed significant strong correlation with the number of contacts, positive in VP, but negative in KP, and with total CDF, negative in VP, but positive in KP (Tables 5 and 6). Stiffness correlated with the number of contacts only in KP, strongly and negatively.

Number of contacts showed very strong negative correlation with all geometric components, but only in KP (Table 5). Very strong negative correlation was found between the contact numbers and all parameters related to cement-endplate distances in VP, and partly in KP.

Correlation of opposite sign was found for VP and KP between failure load and cement distances, CDFs and number of contacts

Table 3
Correlation of failure load, failure displacement and elastic stiffness of VP and KP treated vertebrae with their donor, augmentation and embedding data. Notation for significance: one star: $0.01 \leq P \leq 0.05$; two stars: $0.001 \leq P < 0.01$; three stars: $0.0001 \leq P < 0.001$, four stars: $P < 0.0001$. The abbreviations are as follows: vBMD: volumetric bone mineral density, CVF: cement volume fraction, CAF: cement area fraction, CHF: cement height fraction, CDF: cement distance fraction.

Paired analysis	Failure load				Failure displacement				Elastic stiffness			
Number of pairs: 38	VP		KP		VP		KP		VP		KP	
	R	P	R	P	R	P	R	P	R	P	R	P
Age of subjects	–		−0.501	**	–		–		−0.449	*	−0.453	**
Mean volumetric BMD	–		0.503	**	–		–		–		0.436	*
Vertebral area												
Superior	0.554	**	0.592	**	0.332	*	–		0.455	*	0.524	**
Inferior	0.653	***	0.634	***	0.446	*	0.405	*	0.466	**	0.493	**
Central	0.574	**	0.676	***	0.340	*	–		0.508	**	0.618	***
Vertebral height												
Sagittal anterior	0.393	*	0.435	*	–		–		0.504	**	0.364	*
Sagittal posterior	–		0.359	*	–		0.464	*	–		–	
Sagittal central	–		0.466	*	–		0.362	*	–		0.354	*
Mean sagittal	0.333	*	0.476	*	–		0.479	*	0.348	*	0.344	*
Coronal peripheral	0.453	*	0.500	**	–		–		0.379	*	0.464	*
Coronal central	–		0.387	*	–		0.387	*	–		–	
Mean coronal	0.326	*	0.485	**	–		0.353	*	–		0.386	*
Mean peripheral	0.422	*	0.495	**	–		0.359	*	0.386	*	0.402	*
Mean central	–		0.444	*	–		0.451	*	–		–	
Mean total	0.340	*	0.492	**	–		0.423	*	–		0.374	*
Vertebral width												
Sagittal superior	0.540	**	0.555	**	0.342	*	–		0.464	*	0.554	**
Sagittal inferior	0.588	**	0.553	**	0.376	*	0.369	*	0.498	**	0.480	*
Sagittal central	0.522	**	0.558	**	–		–		0.490	**	0.524	**
Mean sagittal	0.559	**	0.569	**	0.337	*	–		0.498	**	0.533	**
Coronal superior	0.577	**	0.594	**	0.325	*	–		0.491	**	0.543	**
Coronal inferior	0.534	**	0.659	***	0.320	*	–		0.451	*	0.533	**
Coronal central	0.553	**	0.599	***	–		–		0.518	**	0.585	**
Mean coronal	0.568	**	0.642	***	0.321	*	–		0.506	**	0.587	**
Vertebral volume	0.586	**	0.657	***	0.374	*	–		0.489	*	0.565	**
Cement												
Volume fraction, CVF	−0.546	**	−0.660	***	−0.330	*	−0.357	*	−0.473	*	−0.550	**
Max. area	–		0.597	**	–		–		–		0.449	*
Max. area fraction, CAF	−0.553	**	−0.369	*	−0.371	*	–		−0.466	*	−0.353	*
Max. height	0.609	**	–		0.512	**	–		–		–	
Max. height fraction, CHF	0.451	*	−0.379	*	0.405	*	–		–		–	
total distance to endplates	−0.404	*	0.413	*	−0.377	*	–		–		–	
Superior distance	−0.469	*	–		–		–		–		–	
Inferior distance	–		0.359	*	−0.331	*	0.358	*	–		–	
Total distance fraction, CDF	−0.451	*	0.379	*	−0.405	*	–		–		–	
Superior CDF	−0.485	*	–		–		–		–		–	
Inferior CDF	–		–		−0.360	*	0.330	*	–		–	
Number of contacts	0.409	*	−0.488	*	–		–		–		–	
Embedment	–		–		–		–		–		–	
Failure load					0.574	**	–		0.626	***	0.800	****
Failure displacement	0.574	**	–						–		–	
Elastic stiffness	0.626	***	0.800	****	–		–					

Table 4
The effect of contact between cement clouds and endplates on the compressive strength, stiffness and deformability of VP and KP treated vertebrae. Mean values with +/− SD are indicated. The abbreviations are as follows: vBMD: volumetric bone mineral density, CDF: cement distance fraction, CVF: cement volume fraction.

Cement	VP								
Contacts with endplates	n	vBMD mg/cm^3	Superior CDF%	Inferior CDF%	Total CDF%	CVF%	Failure load N	Failure displ. mm	Elastic stiffness N/mm
No contact	3	97 ± 29	7.7 ± 4.6	18.8 ± 5.4	26.5 ± 6.9	17.3 ± 3.1	3749 ± 775	2.09 ± 0.56	4011 ± 1960
1	6	115 ± 44	6.1 ± 4.5	12.6 ± 7.8	18.6 ± 7.0	17.8 ± 5.1	4373 ± 1868	3.03 ± 1.18	3601 ± 912
2	16	102 ± 22	0.8 ± 2.3	13.4 ± 4.8	14.2 ± 4.5	15.0 ± 2.2	5305 ± 996	2.49 ± 0.63	4969 ± 1660
3	10	103 ± 27	0.2 ± 0.6	5.3 ± 2.6	5.4 ± 2.3	18.9 ± 6.1	5562 ± 1756	2.90 ± 0.75	4753 ± 1487
4	3	78 ± 2	0 ± 0	0 ± 0	0 ± 0	20.1 ± 4.0	6013 ± 429	3.12 ± 0.79	4768 ± 2210
Contact	35	102 ± 28	1.4 ± 3.2	9.8 ± 6.6	11.2 ± 7.2	17.0 ± 4.5	5279 ± 1412	2.75 ± 0.80	4655 ± 1567
Total	38	102 ± 27	1.9 ± 3.6	10.5 ± 6.9	12.4 ± 8.3	17.0 ± 4.4	5158 ± 1428	2.70 ± 0.79	4605 ± 1580
Cement	KP								
Contacts with endplates	n	vBMD mg/cm^3	Superior CDF%	inferior CDF%	Total CDF%	CVF%	Failure load N	Failure displ. mm	Elastic stiffness N/mm
No contact	14	113 ± 38	11.7 ± 5.1	20.9 ± 6.1	32.7 ± 8.4	13.9 ± 2.5	5691 ± 1490	3.14 ± 0.66	4259 ± 1294
1	8	103 ± 20	4.7 ± 1.2	23.7 ± 3.8	28.4 ± 4.0	15.0 ± 1.6	5096 ± 855	3.31 ± 0.62	3795 ± 861
2	13	97 ± 27	0.6 ± 2.3	18.2 ± 8.6	18.8 ± 7.9	21.0 ± 4.2	4378 ± 1541	2.91 ± 0.73	3696 ± 1604
3	3	73 ± 9	4.0 ± 3.6	1.1 ± 1.9	5.1 ± 1.8	24.9 ± 4.6	3263 ± 835	2.45 ± 0.79	2920 ± 640
4	0	–	–	–	–	–	–	–	–
Contact	24	96 ± 45	2.4 ± 2.9	17.9 ± 9.6	20.3 ± 9.6	19.5 ± 4.9	4478 ± 1361	2.98 ± 0.73	3632 ± 1296
Total	38	103 ± 31	5.8 ± 5.9	19.1 ± 8.4	24.9 ± 10.8	17.4 ± 5.0	4925 ± 1511	3.04 ± 0.70	3863 ± 1314

both in the paired analysis (Table 3) and when re-grouping the samples according to number of contacts (Table 6). The contact-based analysis showed very strong positive correlation for the failure load, failure displacement and stiffness with bone density in KP, but not in VP (Table 6). Failure load and stiffness showed very strong positive correlations with all morphometric parameters and negative correlation with CVF in KP, but not in VP. Failure load correlated strongly with stiffness only in KP.

Failure occurred inferior to the cement in 55% of VP and 18% of KP specimens; superior to the cement in 8% of both VP and KP; both superior and inferior to the cement in 37% of VP and 74% of KP. In VP, the failure generally occurred along the width of vertebrae, while in most samples of KP, failure was concentrated around the cement clouds (Fig. 2).

4. Discussion

We found no significant differences in failure load between VP and KP (on average 5% larger in VP), stiffness was significantly larger in VP (but only by 19%), failure displacement was non-significantly smaller in VP (by 11%, Table 2). The post-operative CT scans revealed that, as a consequence of the method of KP-augmentation, the cement clouds were more isolated from the bone compared to VP, indicated also by the significantly larger inferior cement-free distances in KP compared to VP. These suggested that the KP augmentation technique resulted in a bone-cement-bone layered structure. These were supported by the mechanical results, i.e. the positive correlation of failure load with all vertebral height components and with the significantly larger inferior cement-free distances in KP compared to VP (Table 1), moreover, the missing correlation with cement height in KP compared to VP in paired analysis (Table 3). The same was confirmed by the result that in KP, the failure displacement was proportional to the vertebral height and inferior cement-free distance, regardless of the height of incompressible cement.

Further analysis provided insights into relationship between the cement-endplate distances and contacts and the mechanical properties. For the comparison with the mechanical results, we attempted to find a single parameter that could represent the fundamentally different method of augmentation and position of cement clouds in both VP and KP and the influences of vertebral geometry and bone density. Since the cement-free distances have important role in the comparison of VP and KP, it could have been chosen as the basis of the detailed analysis. However, our assessment indicated that the cement-free distance measures included more uncertainties compared to the cement-endplate contacts. First, the existence of cement-endplate contacts could be observed more clearly and evaluated more correctly in the CT scans compared to the measures of distances, mainly due to the irregular surface of the clouds. Secondly, the vertical positions of the left and right clouds were not identical, that is, their distances from an endplate were different. Since there was a strict correlation between the distances and the contacts, we decided to perform the analysis rather in terms of the contacts. Thus, we selected the number of cement-endplate contacts as the single common indicator, which highlighted interesting differences between the two treatments.

Whereas the load at failure load in VP increased, in the case of KP it decreased with increasing contact number. These results for VP are in line with the findings of the finite element simulation study of Chevalier et al. [51], who analyzed the biomechanical effect of cement-endplate contacts for VP treatment, reporting that cement contacting one endplate yielded two times stiffer, bridging both endplates 1–8 times stiffer and 1–12 times stronger vertebrae compared to the non-augmented models. They concluded that by establishing cement bridges between the endplates, the cortex is unloaded and greater increase in strength and stiffness can be achieved, while with partial filling the increase was limited as damage localized above or below the augmentation. The biomechanical superiority of endplate-to-endplate filling in VP has also been demonstrated experimentally for non-fractured vertebrae by Kinzl et al. [52]. We obtained similar results for VP, but opposite behavior for KP. In our opinion, the reason is the fundamental difference in the injection technique between VP and KP.

In prophylactic VP of a non-fractured vertebra, the cement has to flow through the inter-trabecular space and results in diffuse clouds having a continuous transition between the augmented and non-augmented bone regions. This yields smoother force transmission with smaller stress concentrations at the interface. The dominant failure occurs below the cement, generally along the width of the vertebra, in the relatively thick non-augmented bone region. (Fig. 2a, c, and e). This is why in VP, failure load decreases with increasing cement-free distances and decreasing number of contacts.

In the case of prophylactic KP, on the other hand, the cement cloud remains concentrated in the cavity prepared by the balloon,

Table 5
Correlation of the contact groups of VP and KP treated vertebrae with their donor, augmentation and embedding data. Notation for significance: one star: $0.01 \le P \le 0.05$; two stars: $0.001 \le P < 0.01$. The abbreviations are as follows: vBMD: volumetric bone mineral density, CVF: cement volume fraction, CAF: cement area fraction, CHF: cement height fraction, CDF: cement distance fraction.

Number of contacts Number of contact groups	VP $n=5$		KP $n=4$	
	R	P	R	P
Age	–		–	
Volumetric BMD, mean	–		−0.959	*
Vertebral area				
Superior	–		−0.977	*
Inferior	–		−0.990	**
Central	–		−0.978	*
Vertebral height				
Sagittal anterior	–		−0.939	*
Sagittal posterior	–		−0.944	*
Sagittal central	−0.833	*	−0.924	*
Mean sagittal	−0.842	*	−0.942	*
Coronal peripheral	–		−0.987	**
Coronal central	–		–	
Mean coronal	–		−0.952	*
Mean peripheral	–		−0.978	**
Mean central	–		−0.906	*
Mean total	–		−0.949	*
Vertebral width				
Sagittal superior	–		−0.977	*
Sagittal inferior	–		−0.999	10^{-10}
Sagittal central	–		−0.975	*
Mean sagittal	–		−0.988	**
Coronal superior	–		−0.952	*
Coronal inferior	–		−0.979	*
Coronal central	–		−0.951	*
Mean coronal	–		−0.966	*
Vertebral volume	–		−0.985	**
Cement				
Volume fraction, CVF	–		0.974	*
Maximum area	–		–	
Maximum area fraction, CAF	–		–	
Maximum height	0.981	**	0.985	**
Maximum height fraction, CHF	0.996	***	0.974	*
Total free distance to endplates	−0.993	***	−0.979	*
Distance to superior endplate	−0.925	*	–	
Distance to inferior endplate	−0.961	*	–	
Total free distance fraction, CDF	−0.996	***	−0.974	*
Superior CDF	−0.921	*	–	
Inferior CDF	−0.962	*	–	
Embedment, mean thickness	–		–	
Failure load	0.981	**	−0.989	**
Failure displacement	–		–	
Elastic stiffness	–		−0.957	*

not interdigitating with trabecular bone. Therefore, the load bearing system of KP resembles a separated bone-cement-bone structure with stress peaks arising directly at the interface due to the non-smooth load transition between the two different materials. Moreover, during balloon inflation, the cancellous bone is compressed and its density increases; but it may be damaged directly at the bone-cement interface. Therefore, failure occurs predominantly in the vicinity of the stiff cement clouds (Fig. 2b, d, and f). Our results indicate also that strength in KP is determined predominantly by vertebral geometry and density; and thus the number of contacts is an indirect measure representing this relationship. Namely, due to the fixed volume of the inflated balloon and injected cement, the number of contacts strongly depends on the vertebral volume and bone density: smaller size and/or weaker bone result in more contacts and smaller cement-free distances (Table 5). Consequently, more contacts and smaller cement-free distances are associated with lower failure strength and stiffness (Table 6). That is why in KP, the failure load increases with decreasing number of contacts and increasing cement-free distances.

The aim of prophylactic augmentation is to increase the strength of intact, but weak vertebrae without excessive increase of stiffness. We found significantly larger stiffness in VP than in KP, but only by 19% (Table 2), and strong positive correlation between strength and stiffness in the paired analysis (Table 3). However, in the contact-based analysis, there was no significant correlation between these properties in VP, while the positive correlation in KP was even stronger than in the paired analysis (Table 6). In KP, similarly to failure load, stiffness increased with decreasing number of contacts and increasing total cement-free distances (Tables 4–6). The increase was 27% in strength and 17% in stiffness in the no-contact cases compared to the contact cases. However, in VP, stiffness showed no clear dependence on the number of contacts, although strength increased significantly (Tables 5 and 6). When compared to specimens with no contacts, strength was 41% greater and stiffness was 16% greater in the contact cases (Table 4).

Besides the analysis of the cement-endplate contact, it is important to mention that in VP the cement spread in all directions, generally flowed against the anterior cortical wall in sagittal direction and got in contact also with the endplates (Fig. 1). Indeed, we observed that both cement clouds contacted the anterior cortical wall in 97% of VP, but only in 50% of KP. These contacts with the front cortical wall and endplates in combination may be the explanation for the higher stiffness of VP-augmented vertebrae observed in the paired analysis (Table 2). The lack of correlation between strength and stiffness in the contact-based analysis in VP (Table 6) suggests that this interaction must influence the stiffness in VP. Indeed, in no-contact and one-contact cases, mainly the reinforced cortical wall seemed to work, while in the cases of higher contact numbers, both the wall- and endplate-contacts appeared to have a mechanical contribution and thus the stiffness increased (Table 4). In turn, in KP, where the cement clouds did not contact the cortical wall significantly, the above effects could not be observed.

Not all combinations of post-fracture and prophylactic augmentation techniques may be reasonable in clinical application. Namely, prophylactic KP is usually not applied with post-fracture VP or even with post-fracture KP, since it is expensive and there is no need for height reconstruction in non-fractured vertebrae. In turn, prophylactic VP with post-fracture VP is often used. Indeed, by biomechanical comparison of post-fracture and prophylactic VP, Furtado et al. [37] concluded that prophylactic augmentation increased failure strength, while stiffness was maintained. Kobayashi et al. [31] found that prophylactic VP prevented AVF for osteoporotic patients. Similarly, Kamano et al. [32] found for prophylactic VP that there was no increased risk of subsequent AVF.

Limitations of this study include the biomechanical testing setup that produced an oversimplified loading case, which may not represent the physiological conditions. In particular, the vertebrae were isolated, embedded in PMMA resin and loaded under constrained uniaxial compression, not allowing typical wedge-shape fractures to develop. The PMMA endcaps may induce different loading transmission compared to intervertebral discs and protect the endplate from stresses. However, these ensured reproducible loading conditions for all samples of both treatment groups. Moreover, due to the parallel loading plates of the testing device the effect of the anterior-posterior positions of the cement column could not be analyzed. Furthermore, the thickness of the embedment of the specimens was not perfectly equal, and the experimental boundary conditions may influence the measured values, mainly for cellular structures. In our earlier study performed on a smaller sample set [53], the effect of embedding thickness was analyzed for VP and KP treated vertebrae, suggesting that it should approximately be kept constant. This effect could be overcome in the present study by increasing the number of specimens. Consequently, there was no significant correlation of strength and

Table 6

Correlation of failure load, failure displacement and elastic stiffness with donor, augmentation and embedding data for contact groups of VP and KP treated vertebrae. Notation for significance: one star: 0.01 $\leq P \leq$ 0.05; two stars: 0.001 $\leq P <$ 0.01. The abbreviations are as follows: vBMD: volumetric bone mineral density, CVF: cement volume fraction, CAF: cement area fraction, CHF: cement height fraction, CDF: cement distance fraction.

Cement-endplate	Failure load				Failure displacement				Elastic stiffness			
Contact analysis	VP		KP		VP		KP		VP		KP	
Number of contact groups	$n=5$		$n=4$		$n=5$		$n=4$		$n=5$		$n=4$	
	R	P	R	P	R	P	R	P	R	P	R	P
Age	–		–		–		−0.970	*	–		–	
Volumetric BMD	–		0.988	**	–		0.908	*	–		0.993	**
Vertebral area												
Superior	–		0.948	*	–		–		–		0.873	*
Inferior	–		0.970	*	–		–		–		0.909	*
Central	–		0.969	*	–		0.897	*	–		0.897	*
Vertebral height	–		0.970	*	−0.880	*	0.970	*	–		0.907	*
Vertebral width												
Mean sagittal	–		0.940	*	–		–		–		0.905	*
Mean coronal	–		0.970	*	–		–		–		0.870	*
Vertebral volume	–		0.973	*	–		–		–		0.906	*
Cement												
Volume fraction, CVF	–		−0.977	*	–		−0.939		–		−0.912	*
Max. area	–		–		–		0.901	*	–		–	
Max. area fraction, CAF	–		−0.988	**	–		–		–		−0.958	*
Max. height	0.990	***	−0.998	***	–		−0.893	*	–		−0.989	**
Max. height fraction, CHF	0.968	**	−0.995	**	–		−0.944	*	–		−0.966	*
Total distance to endplates	−0.967	**	0.995	***	–		0.943	*	–		0.958	*
Superior distance	−0.977	**	–		–		–		−0.869	*	–	
Inferior distance	−0.898	*	0.910	*	–		0.982	**	–		0.894	*
Total distance fraction, CDF	−0.968	**	0.995	**	–		0.944	*	–		0.966	*
Superior CDF	−0.974	**	–		–		–		−0.892	*	–	
Inferior CDF	−0.896	*	0.896	*	–		0.970	*	–		0.890	*
Number of contacts	0.981	**	−0.989	**	–		–		–		−0.957	*
Embedment	–		–		–		–		–		–	
Failure load					–		0.909	*	–		0.978	*
Failure displacement	–		0.909	*					–		–	
Elastic stiffness	–		0.978	*	–		–					

stiffness with the embedding thickness either in VP or in KP groups.

A further limitation was the quasi-static and monotonic loading condition. However, we wanted to investigate the monotonic reaction of the cement clouds inside the vertebrae for all 76 specimens. Further, cyclic testing of this large number of specimens would not have been feasible given the available resources and time for this study.

A limitation can be that the vast majority of vertebrae were harvested from the lumbar spine whereas osteoporotic fractures are likely to occur in the thoracic part. However, in the National Center for Spinal Disorders in Budapest, Hungary, where the specimens were prepared, approximately equal number of lumbar and thoracic vertebrae are augmented. Moreover, we did not want to mix equal number of samples from the lumbar and thoracic vertebrae since it would have led to the introduction of new variables. This was the reason for using only six thoracic specimens. Further, the analysis of the CT scans of larger vertebrae seemed to be more suitable for the comparison of the different structural construction of the cement clouds of VP and KP, and its mechanical consequences.

In conclusion, we found in pair-wise comparison that prophylactic VP resulted in significantly but only slightly larger vertebral stiffness and approximately equal failure load compared to prophylactic KP. Strength in VP showed an increasing trend, but in KP a decreasing trend with increasing number of cement-endplate contacts. The reasons may be the fundamentally different method of augmentation and the resulting differences in the structure of the bone-cement construct. These results indicate that, while both prophylactic techniques appear to provide similar mechanical benefits, these are differently achieved due to the structural differences. Prophylactic VP with post-fracture VP seems to be advantageous to prevent AVF in osteoporotic vertebrae, since the strength can strongly increase with increasing contacts, but the stiffness does not increase significantly. Similarly, prophylactic KP with postfracture KP may also be advantageous if cement contact with the endplates is avoided because, in such cases, increases in strength can be achieved with only a moderate increase in stiffness. In preventive VP, bridge-like contacts, in preventive KP, central cement position with no contacts seem to be preferable. Computer models may help understanding the reasons behind these distinct optimal locations for the two augmentation approaches and could be cross-validated with the results of the present study. Other future work could investigate and directly compare the biomechanical effect of these different cement placements of the two techniques in motion segments to prevent adjacent vertebral fractures in the vicinity of fractured and cemented vertebrae. Moreover, further studies are required to evaluate if and how these findings can be utilized clinically.

Acknowledgments

This research was supported by the Hungarian National Science Foundation OTKA (grant number K-075018). The authors are grateful to Péter Pál Varga, director of the National Center for Spinal Disorders in Budapest, and to Lajos Borbás and Gábor Szebényi for their help in laboratory experiments.

Competing interests

None declared.

Ethical approval

The study involved human cadaver subjects. The ethical approval was granted by the Ethical Commission of the Semmelweis University of Budapest, Hungary (121/2008).

References

[1] Riggs BL, Melton LJ 3rd. The worldwide problem of osteoporosis: insights afforded by epidemiology. Bone 1995;17:505S–511S.
[2] Johnell O, Kanis JA. An estimate of the worldwide prevalence and disability associated with osteoporotic fractures. Osteoporos Int 2006;17:1726–33.
[3] Galibert P, Deramond H, Rosat P, Le Gars D. Preliminary note on the treatment of vertebral angioma by percutaneous acrylic vertebroplasty. Neurochirurgie 1987;33:166–8.
[4] Deramond H, Depriester C, Toussaint P, Galibert P. Percutaneous vertebroplasty. Semin Musculoskelet Radiol 1997;1:285–96.
[5] Jensen ME, Evans AJ, Mathis JM, Kallmes DF, Cloft HJ, Dion JE. Percutaneous polymethylmethacrylate vertebroplasty in the treatment of osteoporotic vertebral body compression fractures: technical aspects. AJNR Am J Neuroradiol 1997;18:1897–904.
[6] Cortet B, Cotten A, Boutry N, Flipo RM, Duquesnoy B, Chastanet P, et al. Percutaneous vertebroplasty in the treatment of osteoporotic vertebral compression fractures: an open prospective study. J Rheumatol 1999;26:2222–8.
[7] Barr JD, Barr MS, Lemley TJ, McCann RM. Percutaneous vertebroplasty for pain relief and spinal stabilization. Spine (Phila Pa 1976) 2000;25:923–8.
[8] Mathis JM, Barr JD, Belkoff SM, Barr MS, Jensen ME, Deramond H. Percutaneous vertebroplasty: a developing standard of care for vertebral compression fractures. AJNR Am J Neuroradiol 2001;22:373–81.
[9] Phillips FM, Todd Wetzel F, Lieberman I, Campbell-Hupp M. An in vivo comparison of the potential for extravertebral cement leak after vertebroplasty and kyphoplasty. Spine (Phila Pa 1976) 2002;27:2173–8 discussion 8-9.
[10] Mathis JM, Deramond H, Belkoff SM. Percutaneous vertebroplasty. New York, Berlin, Heidelberg: Springer; 2002.
[11] Schmidt R, Cakir B, Mattes T, Wegener M, Puhl W, Richter M. Cement leakage during vertebroplasty: an underestimated problem? Eur Spine J 2005; 14:466–73.
[12] Lieberman IH, Dudeney S, Reinhardt MK, Bell G. Initial outcome and efficacy of "kyphoplasty" in the treatment of painful osteoporotic vertebral compression fractures. Spine (Phila Pa 1976) 2001;26:1631–8.
[13] Garfin SR, Yuan HA, Reiley MA. New technologies in spine: kyphoplasty and vertebroplasty for the treatment of painful osteoporotic compression fractures. Spine (Phila Pa 1976) 2001;26:1511–15.
[14] Theodorou DJ, Theodorou SJ, Duncan TD, Garfin SR, Wong WH. Percutaneous balloon kyphoplasty for the correction of spinal deformity in painful vertebral body compression fractures. Clin Imaging 2002;26:1–5.
[15] Watts NB, Harris ST, Genant HK. Treatment of painful osteoporotic vertebral fractures with percutaneous vertebroplasty or kyphoplasty. Osteoporos Int 2001;12:429–37.
[16] Truumees E. The roles of vertebroplasty and kyphoplasty as parts of a treatment strategy for osteoporotic vertebral compression fractures. Current Opin Orthop 2002;13:193–9.
[17] Karlsson MK, Hasserius R, Gerdhem P, Obrant KJ, Ohlin A. Vertebroplasty and kyphoplasty: new treatment strategies for fractures in the osteoporotic spine. Acta Orthop 2005;76:620–7.
[18] Buchbinder R, Johnston RV, Rischin KJ, Homik J, Jones CA, Golmohammadi K, et al. Percutaneous vertebroplasty for osteoporotic vertebral compression fracture. Cochrane Database Syst Rev 2018 6;11:CD006349. doi:10.1002/14651858.CD006349.pub4.
[19] Bouza C, Lopez T, Magro A, Navalpotro L, Amate JM. Efficacy and safety of balloon kyphoplasty in the treatment of vertebral compression fractures: a systematic review. Eur Spine J 2006;15:1050–67.
[20] McCall T, Cole C, Dailey A. Vertebroplasty and kyphoplasty: a comparative review of efficacy and adverse events. Curr Rev Musculoskelet Med 2008; 1:17–23.
[21] Bliemel C, Oberkircher L, Buecking B, Timmesfeld N, Ruchholtz S, Krueger A. Higher incidence of new vertebral fractures following percutaneous vertebroplasty and kyphoplasty–fact or fiction? Acta Orthop Belg 2012;78:220–9.
[22] Eck JC, Nachtigall D, Humphreys SC, Hodges SD. Comparison of vertebroplasty and balloon kyphoplasty for treatment of vertebral compression fractures: a meta-analysis of the literature. Spine J 2008;8:488–97.
[23] Papanastassiou ID, Phillips FM, Van Meirhaeghe J, Berenson JR, Andersson GB, Chung G, et al. Comparing effects of kyphoplasty, vertebroplasty, and non-surgical management in a systematic review of randomized and non-randomized controlled studies. Eur Spine J 2012;21:1826–43.
[24] Wang H, Sribastav SS, Ye F, Yang C, Wang J, Liu H, et al. Comparison of percutaneous vertebroplasty and balloon kyphoplasty for the treatment of single level vertebral compression fractures: a meta-analysis of the literature. Pain Phys 2015;18:209–22.
[25] Chang X, Lv YF, Chen B, Li HY, Han XB, Yang K, et al. Vertebroplasty versus kyphoplasty in osteoporotic vertebral compression fracture: a meta-analysis of prospective comparative studies. Int Orthop 2015;39:491–500.
[26] Song D, Meng B, Gan M, Niu J, Li S, Chen H, et al. The incidence of secondary vertebral fracture of vertebral augmentation techniques versus conservative treatment for painful osteoporotic vertebral fractures: a systematic review and meta-analysis. Acta Radiol 2015;56:970–9.
[27] Xiao H, Yang J, Feng X, Chen P, Li Y, Huang C, et al. Comparing complications of vertebroplasty and kyphoplasty for treating osteoporotic vertebral compression fractures: a meta-analysis of the randomized and non-randomized controlled studies. Eur J Orthop Surg Traumatol 2015;25(Suppl 1):S77–85.
[28] Kim SH, Kang HS, Choi JA, Ahn JM. Risk factors of new compression fractures in adjacent vertebrae after percutaneous vertebroplasty. Acta Radiol 2004;45:440–5.
[29] Wang YT, Wu XT, Chen H, Wang C, Mao ZB. Adjacent-level symptomatic fracture after percutaneous vertebral augmentation of osteoporotic vertebral compression fracture: a retrospective analysis. J Orthop Sci 2014;19:868–76.
[30] Ning L, Wan S, Liu C, Huang Z, Cai H, Fan S. New levels of vertebral compression fractures after percutaneous kyphoplasty: retrospective analysis of styles and risk factors. Pain Phys 2015;18:565–72.
[31] Kobayashi N, Numaguchi Y, Fuwa S, Uemura A, Matsusako M, Okajima Y, et al. Prophylactic vertebroplasty. Acad Radiol 2009;16:136–43.
[32] Kamano H, Hiwatashi A, Kobayashi N, Fuwa S, Takahashi O, Saida Y, et al. New vertebral compression fractures after prophylactic vertebroplasty in osteoporotic patients. AJR Am J Roentgenol 2011;197:451–6.
[33] Becker S, Garoscio M, Meissner J, Tuschel A, Ogon M. Is there an indication for prophylactic balloon kyphoplasty? A pilot study. Clinical Orthop Rel Res 2007;458:83–9.
[34] Eichler MC, Spross C, Ewers A, Mayer R, Kulling FA. Prophylactic adjacent-segment vertebroplasty following kyphoplasty for a single osteoporotic vertebral fracture and the risk of adjacent fractures: a retrospective study and clinical experience. J Neurosurg Spine 2016;25:528–34.
[35] Higgins KB, Harten RD, Langrana NA, Reiter MF. Biomechanical effects of unipedicular vertebroplasty on intact vertebrae. Spine (Phila Pa 1976) 2003;28:1540–7 discussion 8.
[36] Sun K, Liebschner MA. Biomechanics of prophylactic vertebral reinforcement. Spine (Phila Pa 1976) 2004;29:1428–35 discusssion 35.
[37] Furtado N, Oakland RJ, Wilcox RK, Hall RM. A biomechanical investigation of vertebroplasty in osteoporotic compression fractures and in prophylactic vertebral reinforcement. Spine (Phila Pa 1976) 2007;32:E480–7.
[38] Chiang C-K, Wang Y-H, Yang C-Y, Yang B-D, Wang J-L. Prophylactic vertebroplasty may reduce the risk of adjacent intact vertebra from fatigue injury: an ex vivo biomechanical study. Spine 2009;34:356–64.
[39] Hulme PA, Boyd SK, Heini PF, Ferguson SJ. Differences in endplate deformation of the adjacent and augmented vertebra following cement augmentation. Eur Spine J 2009;18:614–23.
[40] Aquarius R, Homminga J, Hosman AJF, Verdonschot N, Tanck E. Prophylactic vertebroplasty can decrease the fracture risk of adjacent vertebrae: an in vitro cadaveric study. Med Eng Phys 2014;36:944–8.
[41] Kurutz M, Jakab G, Varga P, Varga PP. Biomechanical evaluation of vertebroplasty and kyphoplasty by uniaxial compressive test. Biomech Hung 2013;VI:311–22.
[42] Zou W, Gao J, Jones AS, Hunter N, Swain MV. Characterization of a novel calibration method for mineral density determination of dentine by X-ray micro–tomography. Analyst 2009;134:72–9.
[43] Huang TTY, Jones AS, He LH, Darendeliler MA, Swain MV. Characterisation of enamel white spot lesions using X-ray micro-tomography. J Dent 2007; 35:737–43.
[44] Pisani P, Renna MD, Conversano F, Casciaro E, Muratore M, Quarta E, et al. Screening and early diagnosis of osteoporosis through X-ray and ultrasound based techniques. World J Radiol 2013;5:398–410.
[45] American College of Radiology. ACR Practice Guideline for the Performance of Quantitative Computed Tomography (QCT) Bone Densitometry (Resolution 39). 2008.
[46] Engelke K, Adams JE, Armbrecht G, Augat P, Bogado CE, Bouxsein ML, et al. Clinical use of quantitative computed tomography and peripheral quantitative computed tomography in the management of osteoporosis in adults: the 2007 ISCD official positions. J Clin Densitom 2008;11:123–62.
[47] Ma XH, Zhang W, Wang Y, Xue P, Li YK. Comparison of the spine and hip BMD assessments derived from quantitative computed tomography. Int J Endocrinol 2015;2015:675340.
[48] Campbell MJ. Statistics at square two: understanding modern statistical applications in medicine. London: BMJ Books; 2006.
[49] Swinscow TDV, Campbell MJ. Statistics at square one. London: BMJ Books; 2002.
[50] Simes RJ. An improved Bonferroni procedure for multiple tests of significance. Biometrica 1986;73:751–4.
[51] Chevalier Y, Pahr D, Charlebois M, Heini P, Schneider E, Zysset P. Cement distribution, volume, and compliance in vertebroplasty: some answers from an anatomy-based nonlinear finite element study. Spine (Phila Pa 1976) 2008;33:1722–30.
[52] Kinzl M, Benneker LM, Boger A, Zysset PK, Pahr DH. The effect of standard and low-modulus cement augmentation on the stiffness, strength, and endplate pressure distribution in vertebroplasty. Eur Spine J 2012;21:920–9.
[53] Kurutz M, Nédli P, Varga P, Csákány T, G J. Experimental and numerical analysis of the influence of embedding thickness in compressive mechanical testing of vertebral augmentation and spinal interbody fusion. Biomech Hung 2013;VI:331–44.