Author: Muijs, Sander Paul Jan
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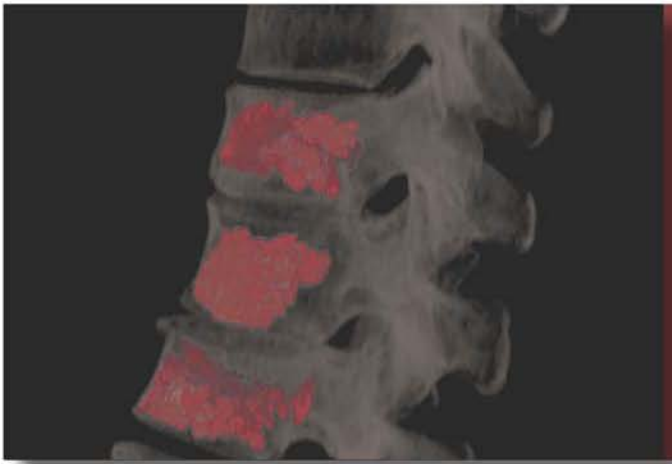
Chapter 6



S.P.J. Muijs[1]
P.D.S. Dijkstra[1]
A.R. van Erkel[2]

[1]Department of Orthopaedic Surgery, Leiden University Medical Center, Leiden, The Netherlands.
[2]Department of Radiology, Leiden University Medical Center, Leiden, The Netherlands.

A system for Evaluation of eXtra vertebral cement leakage in vertebroplasty based on Anatomy and volume in CT-scan analysis; The EXACT classification

Submitted

Abstract

Purpose. The majority of clinically relevant complications after Percutaneous VertebroPlasty (PVP) are due to cement leakage. A radiological classification of these cement leakages should be reproducible precise and logical. The currently used classification systems, provide no information on the anatomical location and volume of the cement leakage, making it impossible to determine which leakages lead to clinically relevant complications.

Aim. The aim of this study is to test a new system for Evaluation of eXtra vertebral cement leakage in vertebroplasty based on Anatomy and volume of the leakage using CT-scan analysis (the EXACT classification system) with superior discrimination potential. This system describes spatial distribution and anatomical structures of the leakage in addition to the Cement Leakage Volume.

Materials and methods. The direct postoperative CT-data of 106 vertebral bodies from 53 patients, treated with PVP were analyzed. Leakages were analyzed according to the system published by Yeom et al., and using the new anatomy based classification system.

Results. The inter-observer variability, using the new scoring system was 0.94 ($p<0.001$), which is comparable to the inter-observer variability of 0.97 ($P<0.001$) found when using the system of Yeom et al. In addition to the leakage volume, the new system identified leakage sites more specific in terms of anatomical and spatial distribution compared to the classification system according to Yeom et al.

Conclusions. The new system facilitates research, investigating divergence in leakage patterns of different cement types available on the market and to register specific cement leakages and possible clinical sequelae.

Introduction

Since Percutaneous VertebroPlasty (PVP) was introduced in 1989 as a minimal invasive procedure for the treatment of painful Osteoporotic Vertebral Compression Fractures (OVCFs), the procedure gained popularity because of its high effectiveness in fast pain reduction.[1] Fast, significant and clinically relevant relief of symptoms and restoration of mobility, is achieved in more than 80% of patients in multiple large studies.[2-4] Moreover, PVP has many advantages compared to extensive surgery due to its minimal invasiveness, and relatively low costs.

Due to two recent randomized blinded controlled trials, which showed no beneficial effect of vertebroplasty compared to a sham procedure, specialists became more alert on possible negative side effects of the procedure.[5,6] The new insights called for more accurate registration of possible negative side effects and complications of the PVP procedure.

The rate of complications with a clinical sequel of PVP is low and is reported to range from 1.6% to 2.8%.[7] The reported complications with PVP in OVCFs however range from apparently clinically silent unanticipated advents to catastrophic clinical outcome and death.[8-11] The vast majority of the clinically relevant complications of PVP are due to leakage of bone-cement. Severe complications are rare and mainly occur in case of high volume cement leakage.

Reported complications include cement entering the nerve root foramen or spinal canal, resulting in radiculopathy or spinal cord compression, embolic events due to marrow fat or cement entering the circulation, malplacement of the needle, rib fractures, pneumothorax, fracture of processus spinosus or pedicle, subcutaneous paravertebral hematoma and infection.[12-18]

In PVP, PolyMethylMethAcrylate (PMMA) bone cement is the most widely used type of cement. There's a wide variety of PMMA cements types with different viscosity available. The viscosity is often categorized as low-viscosity (comparable to yoghurt), medium viscosity (comparable to toothpaste) and high viscosity (comparable to dough). These types of cement are clinically used interchangeably, despite of the fact that literature suggests that there are differences in frequency volume and leakage types between the cement types used.[19,20] Currently, still new types of PMMA cement are introduced to the market without certainty concerning its potential leakage behavior.

So far, accurate and comparable data concerning the risk of clinically relevant complications due to specific cement leakage types are unavailable. This is partly due to a lack of radiological (i.e. CT) follow-up and the lack of a clinically applicable classification system for cement leakages.

The only paper specifically describing and testing a leakage classification system is by Yeom et al in 2003.[18] This classification system, divides cement leakages in Basivertebral (B), Segmental (S) and Cortical (C) but gives no information on the anatomical location and volume of the cement leakage and may therefore lack clinical relevance.

Papers concerning cement leakage describe a variety systems, which are based on the system published by Yeom et al. and show resemblances but are however not similar enough to compare the outcomes in a detailed meta-analysis.[21-26] In order to facilitate more accurate registration of cement leakages, a logical, accurate, and reproducible cement leakage classification system is mandatory.

The aim of the current study was therefore to develop and test a new system for Evaluation of eXtra vertebral cement leakage in vertebroplasty based on Anatomy and volume of the leakages using CT-scan analysis (EXACT system). This system describes spatial distribution (anterior (A.x.x), medial (B.x.x) or posterior (C.x.x)) and anatomical structures (venous system (x.1.x), cortical defect (x.2.x)) of the leakage and specific sites (e.g. vein or discus) in addition to the cement leakage volume (x.x.0.5cc)(**Figure 1**). For venous leakages (x1x), 5 types are recognized by their anatomical location (anterior external plexus, the basivertebral vein, the segmental vein, the anterior internal plexus and the posterior internal plexus (**Figure 2**), a comprehensive description of the vertebral venous structures has previously been published by Groen et al.[27]

	A ANTERIOR	B CENTRAL	C POSTERIOR
X.1.X VENOUS	A*1* *Venous*	B*1* *Venous*	C*1* *Venous*
	A1.*1* Anterior External venous *P*lexus (*AEP*)	B1.*1* Basivertebral *V*ein (*BV*)	C1.*1* *A*nterior *I*nternal venous *P*lexus (*AIP*)
		B1.2 Segmental vein (*SV*)	C1.2 Posterior *I*nternal venous *P*lexus (*PIP*)
X.2.X CORTICAL	A2 *Cortical*	B2 *Cortical*	C2 *Cortical*
	A2.*1* Single anterior leak	B2.*1* Superior endplate # / superior discal leak	C2.*1* Posterior wall corpus
	A2.2 Multiple anterior leak	B2.2 Inferior endplate # / Inferior discal leak	C2.2 Medial pedicle wall
		B2.3 Lateral leak	C2.3 Neelde traject
LEAKAGE	Ax.x._CC	B x.x._CC	Cx.x._CC

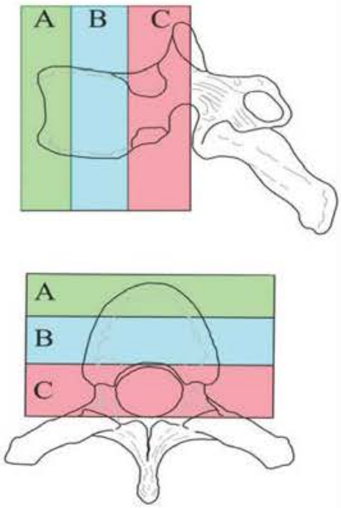


Figure 1. Overview of the EXACT anatomy based scoring system.

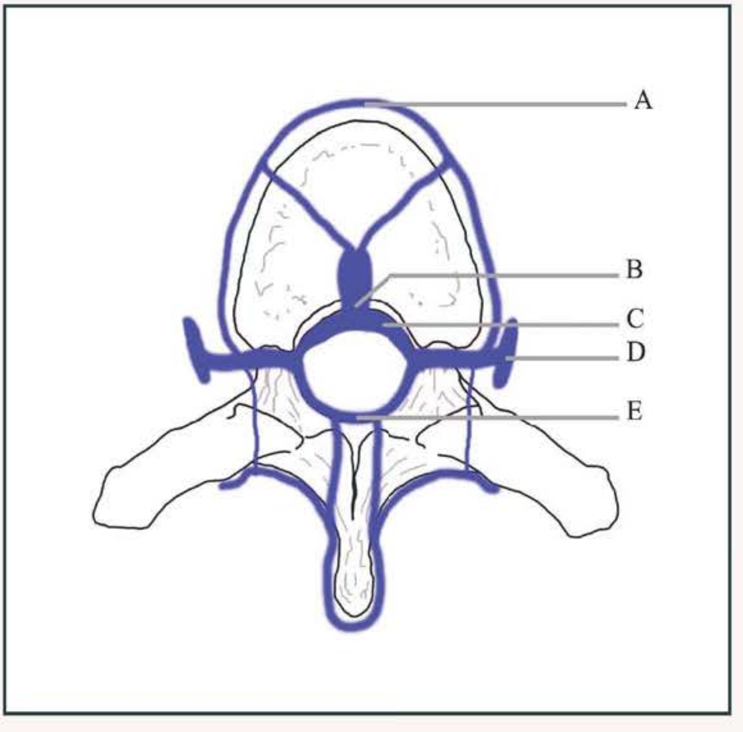


Figure 2. Shows a schematic drawing of the anatomy of the vertebral venous system. A; Anterior External Plexus (AEP), B: Basivertebral Vein (BV), C: Anterior Internal Venous Plexus (AIP), D: Segmental Vein (SV), E: Posterior Internal Venous Plexus (PIP).

Patients and Methods

Data were collected from 53 patients treated for 106 painful OVCFs between January 2008 and January 2009. All patients underwent a post-intervention CT-scan using a standardized protocol and a standard multi-slice CT-scanner (Thoshiba Aquilion 64 slice, slice thickness: 1.0mm, Gantry-tilt: 0 degrees, X-ray tube kilovoltage (KVP) 135, X-ray tube current 250, Exposure time 500)

The 106 vertebral bodies (VB) from 53 patients were divided into three regions. 1) Thoracic region, in which T5-T10 were grouped, (37 VB (34.9%)), 2) Thoraco-lumbar region, in which T11-L2 were grouped, (50 VB (47.2%)), and 3) Lumbar region in which L3-L5 were grouped (19 VB (17.9%)).

Calibration

The direct postoperative CT-data of the 106 vertebral bodies (VB) treated with PVP were analyzed using a calibrated DICOM viewer (Osirix 3.3, 64 bit, Kagi, Berkeley, California). The Osirix DICOM viewer was calibrated by CT-analysis of cement volumes injected in 8 cadaveric pig vertebrae, which were hermetically sealed in a container of gelatin and scanned on the same CT-scanner, which was used during the clinical experiment. The analyzed vertebral bone was dissolved in hydrochloric acid and the volume of the remaining PMMA-cement was determined by water-displacement volumetry. After measurement of the actual, in vitro, cement-volume, 3D growing region segmentation was calibrated using a fixed lower pixel threshold of 100, and a fixed upper threshold of 10.000. This wide window could be used due to the high difference in opacity of the opacified bone-cement compared to the surrounding vertebral bone. All specimens were tested and all volumes were calculated 4 times. After calibration, the CT-analysis was found to be accurate up to 0.01mL of PMMA cement.

Analysis of CT-data

Analysis of the CT-data acquired from the treated patients in our cohort included: 1) vertebral level; 2) Cement Leakage Volume, defined as the total cement volume outside of the cortical border of a treated vertebral body and is acquired by adding the volume of all solitair cement leakages in a single treated vertebral body; 3) Total Cement Volume , defined as the total volume of cement within the vertebral body (including the volume trabecular bone captured within the injected cement) and outside the cortical boundaries of the vertebral body; 4) cement leakage classification according to Yeom et al.; and 5) cement leakage classification acc. to the new classification system. All vertebral levels were graded by 3 independent observers experienced in assessing skeletal CT-scans, using both the classification system according to Yeom et al. and the new classification system.

Statistical Analysis

A probability value of <0.05 (two-tailed) was considered statistically significant. The intra-class correlation coefficient for leakage category scoring was tested for absolute agreement using a two-way mixed model where people effects are random and measures effects are fixed in SPSS statistical software 16.0, (SPSS Inc, Chicago, IL).

Results

Classification according to the EXACT system showed a total of 124 leakages. In the thoracic region, 46 leakages were detected (1.24 leakage sites/VB). Mean cement leakage volume in the thoracic region was 0.33 mL and ranged from 0.02 to 1.76 mL. In the thoraco-lumbar, region 61 leakages were detected (1.24 leakage sites/VB). Mean cement leakage volume in the thoraco-lumbar region was 0,47 mL (range 0.02-5.59 mL). In the lumbar region 17 leakages were detected (0.89 leakage sites/VB). Mean cement leakage volume the lumbar region was 0,32 (range 0.02-3,61 mL). Of all leakages, 53 (43%) consisted out of a cement volume ≥ 0.25 mL and 28 (23%) out of ≥ 0.5 mL. Of these larger leakages, 38 (72%) were located through the superior and inferior endplates B2.1 and B2.2, and 9 (17%) into the anterior internal plexus C1.1 (**Table1, Figure 3**). Mean total cement volume was: 3.82 ±1.45 mL in the thoracic region, 5.26 ±2.04 mL in the thoraco-lumbar region and 6.57±2.15 mL in the lumbar region.

Classification of the leakages according to the classification system of Yeom et al. also showed 124 leakage sites of which 30 type B (Basivertebral vein leakage), 29 type S (segmental vein leakage) and 65 type C (Cortical defect). **Table 2** demonstrates the subdivision of cortical and venous leakages in relation to the system of Yeom et al.

The inter-observer variability (intra-class observer correlation) of 3 independent observers for the EXACT classification system, was 0.94, the inter-observer variability when using the classification system according to Yeom et al. was 0.97 ($P<0.001$).

	Yeom et al.			Current study											
	B	S	C	A 1.1	A 2.1	A 2.2	B 1.1	B 1.2	B2.1	B2.2	C1.1	C1.2	C2.1	C2.2	C2.3
T	11	9	26	6	1	1	1	4	13	10	9	1	0	0	0
TL	15	14	32	7	3	1	0	6	15	13	14	0	0	0	0
L	4	6	7	2	1	0	0	3	1	4	4	1	0	0	2
	30 (24%)	29 (23%)	65 (52%)	16 (13%)	5 (4%)	2 (2%)	1 (1%)	13 (10%)	29 (24%)	27 (22%)	29 (22%)	0 (2%)	0 (0%)	0 (0%)	2 (2%)

Table 1. Cement leakage per region according to Yeom et al. and the EXACT classification system. (T=thoracic region,TL= thoracolumbar region, L= lumbar region).

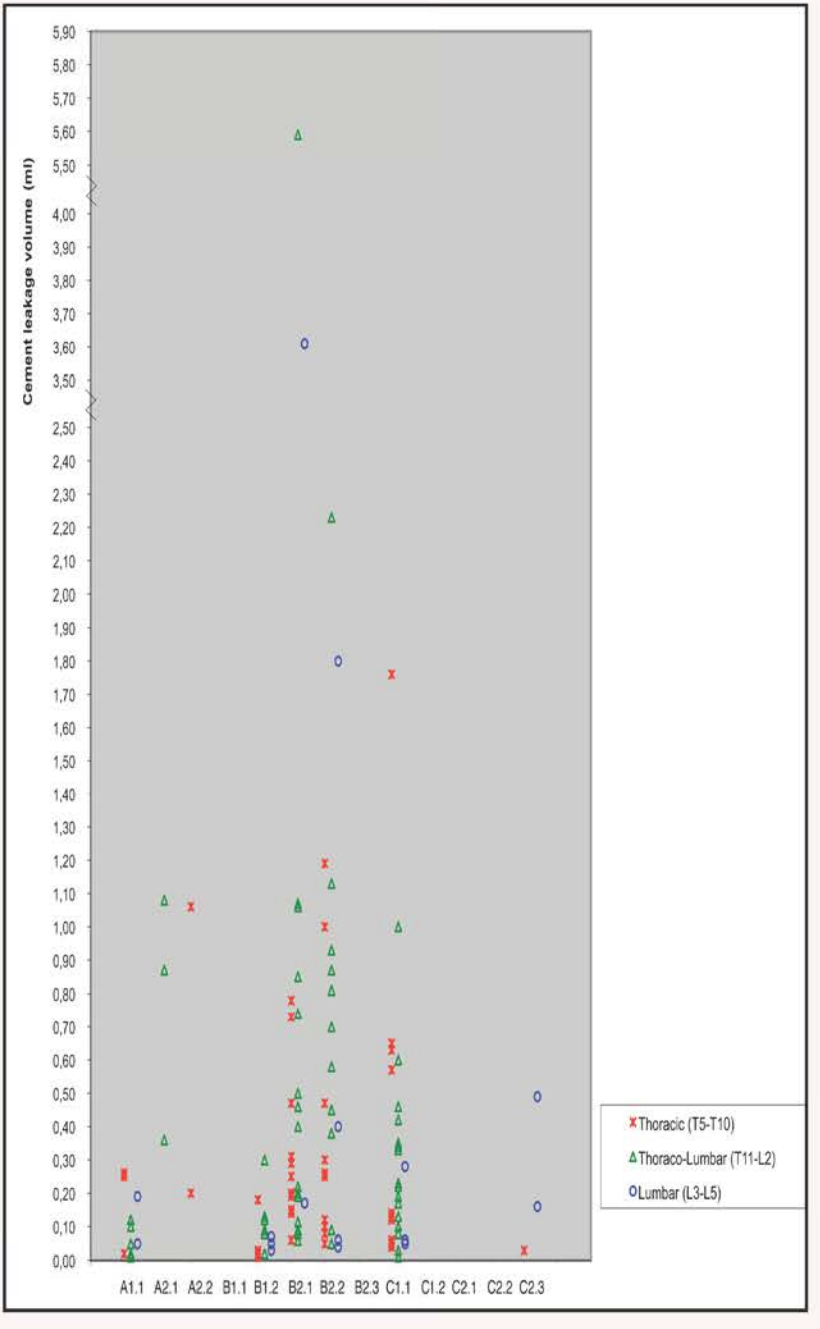


Figure 3. Cement leakage volume (mL) per anatomical class according to the EXACT system.

anatomy based system	Basivertebral (B)	Segmental (S)	Cortical (C)
a1.1 Anterior external venous plexus		16	
a2.1 Singe anterior leak (cortical)			5
a2.2 Multiple anterior leak (cortical)			2
b1.1 Basivertebral vein	1		
b1.2 Segmental vein		13	
b2.1 Superior endplate/discus			29
b2.2 Inferior endplate/discus			27
b2.3 Lateral leak (cortical)			
c1.1 Anterior internal venous plexus	27		
c1.2 Posterior internal venous plexus	2		
c2.1 Posterior wall corpus (cortical)			0
c2.2 Medial pedicle wall			0
C2.3 Needle traject			2
	Total 30	Total 29	Total 65

System according. To Yeom et al.

(hatched) Overlap new system and acc. to Yeom et al.

Table 2. Comparison overview of the number and distribution of leakages in the EXACT classification system versus the classification system according to Yeom et al.

Discussion

In 2009, two randomized, blinded, controlled trials, have been published.[5,6] Both trials showed no beneficial effect of vertebroplasty compared to a sham procedure among patients with painful osteoporotic vertebral fractures. An even more recent randomized study however showed that vertebroplasty is superior compared to conservative treatment. The outcome of the former two trials, which showed no beneficial effect of vertebroplasty, made specialists more alert on possible negative side effects of the procedure.[28,29] Because both papers were simultaneously published in the prestigious New England Journal of Medicine, the results had a major effect on physicians, media and public. The new insights called for accurate registration of possible negative side effects and complications of the PVP procedure.

In light of the renewed emphasis on critical judging of complications and possible side-effects of the PVP procedure, research should be conducted using understandable, reproducible and precise outcome measures.

As cement leakage is reported to account for the majority of complications of PVP, and is found in up to 88% of the PVP procedures, the leakages and their sequeale should be registered.[30,31] Cement leakage is dependent on the injected cement volume and is best detected using post-operative CT-scanning.[32] The use of CT scanning versus plain X-ray results in a increase of more than 50% leakage detection.[30] Fluoroscopic or plain radiography imaging, which are often used for assessing cement leakage, are insufficient to collect enough information concerning the effects of the leakages. Both the exact anatomical position as well as the volume of the leakage is very difficult to assess. Schmidt et al. found in their study that the agreement rate between fluoroscopy and CT scans ranged from 66% to 74%, while inter-observer reliability showed only fair agreement. Especially leakages in the basivertebral veins were frequently misinterpreted.[30]

To objectivate the clinical outcome after PVP or other procedures, numerous well-tested questionnaires have been developed over the years (Short-Form 36 (SF36), Roland-Morris disability score, visual analogue score (VAS)).[33-35] However, when investigating the complication rate in PVP, in which the most prevalent complication is cement leakage, there is no classification system to evaluate the clinical consequences of cement leakage.

In vertebroplasty the complication rate is low (1.6% - 2.8%), but mainly due to cement leakage.[7] So far, the "common" cement leakage in PVP, is said to be without clinical consequences in the majority of cases. Clinical relevance of cement leakages is highly dependant on the site of the leakage. Leakage to the neuro-foramen or the spinal canal might result in neurologic complications.[10] Furthermore, leakage to the intervertebral disc could lead to altered biomechanical stress to the adjacent vertebral body and could possibly cause an increased risk of new fractures.[36] Leakages to arterial or venous structures are reported to cause pulmonary embolism, and have been reported to be present in up to 18% of patients after a PVP procedure.[12] Even cardiac perforation and cerebral cement embolism have been reported.[9,12,37] Without a precise system to measure cement leakage in order to correlate these outcomes to possible clinical consequences of these leakages, a good insight in the dangers of cement leakages during PVP can not be made.

When using the classification system published by Yeom et al., leakages of cement are classified into three types: 1) Type B - leakages via the basivertebral vein - these leakages involve leakage of cement into the spinal canal. They proceed via the vascular foramen and in the spinal canal they follow the epidural venous plexus, 2) Type-S - leakages via the segmental vein - these leaks often proceed horizontally, in line of the segmental veins. They therefore often mimic a small paravertebral leak on anteroposterior radiographs. They are, however, often long leaks, and may reach the neural foramina and finally Type-C - through a cortical defect around a vertebral body, including the spinal canal. Leaks into the spinal canal for example therefore may be scored as a type-B or type-C leakage, when using the system according to Yeom et al.[18] No information concerning the anatomical position or the volume of the leakage is provided using the aforementioned system. Moreover, cortical leakage (C) in the system of Yeom et al. are grouped in one category, hereby discarding all information concerning structures which could be at risk at specific sites.

When using the EXACT system, in which not only insight concerning the specific anatomical position of a leakage is added to the classification but also the leakage volume. All information about spatial distribution (anterior (A.x.x), medial (B.x.x) or posterior (C.x.x)) and anatomical structures (venous system (x.1.x), cortical defect (x.2.x)) of the leakage and specific sites (e.g. vein or discus) and the cement leakage volume (x.x.0.5 mL) are combined into one classification. Due to the anatomical description of the leakage combined with a spatial classification, a more accurate registration of leakages is possible (**Figure 4**).

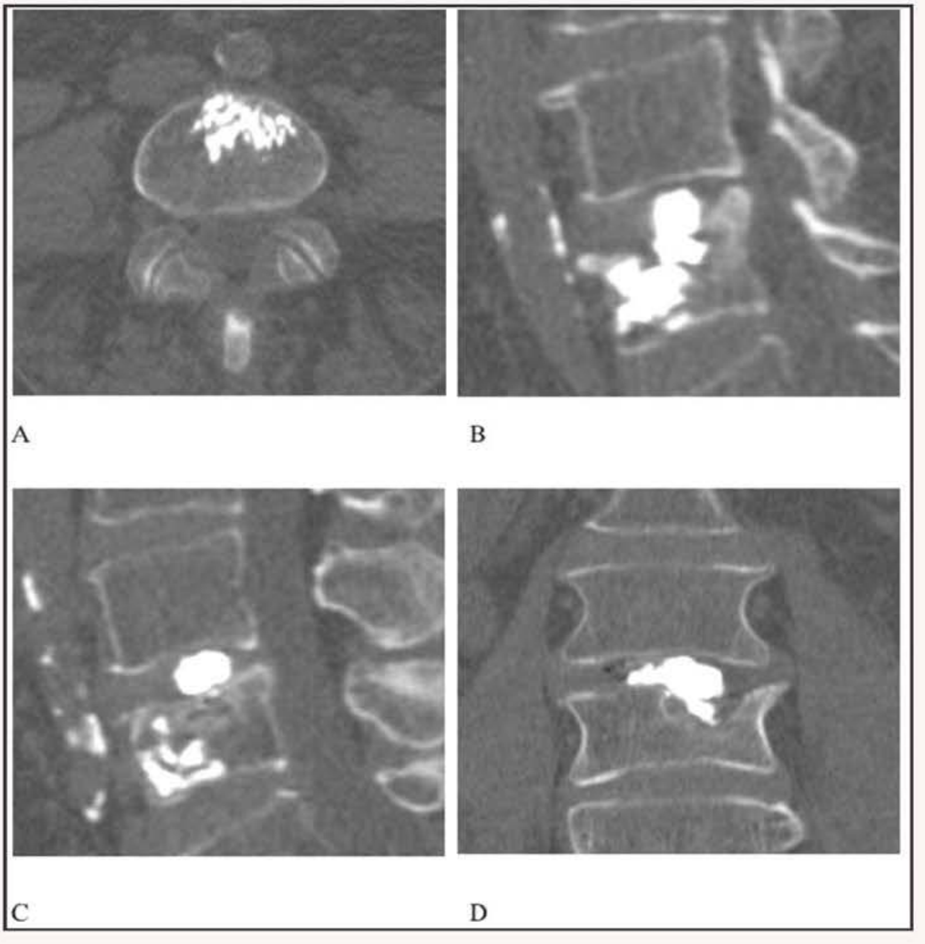


Figure 4. Shows the practical implementation of the new classification system. **A**: axial image of the treated corpus shows no venous leakage and no leakage through the anterior, lateral or posterior cortex. **B** and **C**: sagittal images show a leakage through the superior endplate into the discus (3.6 mL). **D**: coronal reconstruction shows the leakage centrally through the superior endplate. When using the system of Yeom et al. and thus neglecting were the leak penetrates through the cortical bone, the fact that it concerns a high-volume discus leakage, this leakage would be a type C. According to the EXACT classification this leakage would be a B-2-1-3.6 mL.

The current study showed that, when using the EXACT system, the majority of larger leakages (≥0.5 mL) occur through the endplates into the intervertebral disc, which will lead to altered forces applied to the adjacent levels and possibly even to new vertebral fractures.[38,39] Furthermore in 17% of the leakages ≥0.5 mL, the anterior internal plexus is involved, a structure which is situated within the spinal canal.

As with every classification system, inter-observer variability should be as low as possible. When categories are too much alike, the interobserver variability will rise making the classification system less reliable. The proposed system has, due to its high precision in describing the anatomical and spatial distribution, more categories in which the observer could place a certain cement leakage than in the system published by Yeom et al. The intra-class correlations of the EXACT system (0.94, $p<0.001$) was comparable to the interobserver variability of 0.97 ($P<0.001$) found when using the classification system acc. to Yeom et al.

While this study provides a logical, precise and reproducible new classification system for cement leakages during PVP, some limitations should be noted. This system is only applicable when postoperative CT scans are routinely performed. Some categories (C1.1 and C2.2) in the new system, were not encountered during this study, the authors however feel that if leakages at these sites do occur, a high chance of clinical consequences is to be expected.

Considering that the PVP procedure is being scrutinized due to the publications in NJEM in 2009, combined with the knowledge that there is a lack of adequate data concerning leakage frequency and patterns, the growing evidence on the role of viscosity, and the fact that still new types of PMMA cement are introduced to the market, calls for a reliable registration as is currently done in other types of prosthesis.

When using the EXACT system, leakage sites can be more specifically identified as compared to the classification according to Yeom et al. The EXACT system has an obvious value in research of the PVP procedure and the types of cement used during the procedure. The authors furthermore expect the EXACT classification system to be of greater clinical value. Implementation of the EXACT system and registration of leakages on large scale data facilitates pooling data from different centers and offers the possibility to gain important new insight into which leakages are to be expected to lead to clinically relevant complications and which viscosity types of cement are more likely to result in clinically relevant cement leakages.

References

1. Mottolese C, Deruty R, Lapras C, Remond J, Duquesnel J. Percutaneous injection of methyl-metacrylate in osteoporosis and severe vertebral osteolysis (Galibert's technic). *Annals de chirurgie* 1989. 371-6.
2. McGraw JK, Lippert JA, Minkus KD, Rami PM, Davis TM, Budzik RF. Prospective evaluation of pain relief in 100 patients undergoing percutaneous vertebroplasty: results and follow-up. Journal of vascular and interventional radiology: *JVIR* 2002. 883-6.
3. Kobayashi K, Shimoyama K, Nakamura K, Murata K. Percutaneous vertebroplasty immediately relieves pain of osteoporotic vertebral compression fractures and prevents prolonged immobilization of patients. *Eur Radiol.* 2005. 360-7.
4. Alvarez L, Pérez-Higueras A, Granizo JJ, de Miguel I, Quiñones D, Rossi RE. Predictors of outcomes of percutaneous vertebroplasty for osteoporotic vertebral fractures. *Spine.* 2005. 87-92.
5. Buchbinder R, Osborne RH, Ebeling PR, et al. A randomized trial of vertebroplasty for painful osteoporotic vertebral fractures. *N Engl J Med* 2009. 557-68.
6. Kallmes D, Comstock B, Heagerty P, et al. A Randomized Trial of Vertebroplasty for Osteoporotic Spinal Fractures. *N Engl J Med* 2009. 569.
7. Lee MJ, Dumonski M, Cahill P, Stanley T, Park D, Singh K. Percutaneous treatment of vertebral compression fractures: a meta-analysis of complications. *Spine* 2009. 1228-32.
8. Lim KJ, Yoon SZ, Jeon Y-S, et al. An intraatrial thrombus and pulmonary thromboembolism as a late complication of percutaneous vertebroplasty. *Anesth Analg* 2007. 924-6.
9. Schoenes, Bremerich, Risteski, Thalhammer, Meininger. Cardiac perforation after vertebroplasty. *Anaesthesist* 2007.
10. Patel AA, Vaccaro AR, Martyak GG, et al. Neurologic deficit following percutaneous vertebral stabilization. *Spine* 2007. 1728-34.
11. Eck, Nachtigall, Humphreys, Hodges. Comparison of vertebroplasty and balloon kyphoplasty for treatment of vertebral compression fractures: a meta-analysis of the literature. *Spine J* 2007.
12. Kim YJ, Lee JW, Park KW, et al. Pulmonary cement embolism after percutaneous vertebroplasty in osteoporotic vertebral compression fractures: incidence, characteristics, and risk factors. *Radiology* 2009. 250-9.
13. Birkenmaier C, Seitz S, Wegener B, et al. Acute paraplegia after vertebroplasty caused by epidural hemorrhage. A case report. *The Journal of bone and joint surgery American volume* 2007. 1827-31.
14. Anselmetti GC, Corgnier A, Debernardi F, Regge D. Treatment of painful compression vertebral fractures with vertebroplasty: results and complications. *La Radiologia medica* 2005. 262-72.
15. Baumann C, Fuchs H, Kiwit J, Westphalen K, Hierholzer J. Complications in percutaneous vertebroplasty associated with puncture or cement leakage. *Cardiovascular and interventional radiology* 2007. 161-8.
16. Layton KF, Thielen KR, Koch CA, et al. Vertebroplasty, first 1000 levels of a single center: evaluation of the outcomes and complications. *AJNR* 2007. 683-9.
17. Vats HS, McKiernan FE. Infected vertebroplasty: case report and review of literature. *Spine* 2006. E859-62.
18. Yeom JS, Kim WJ, Choy WS, Lee CK, Chang BS, Kang JW. Leakage of cement in percutaneous transpedicular vertebroplasty for painful osteoporotic compression fractures. *The Journal of bone and joint surgery British volume* 2003. 83-9.
19. Lewis G. Viscoelastic properties of injectable bone cements for orthopaedic applications: State-of-the-art review. *J Biomed Mater Res Part B Appl Biomater* 2011. 171-91.

20. Nieuwenhuijse MJ, Muijs SPJ, van Erkel AR, Dijkstra SPD. A clinical comparative study on low versus medium viscosity polymethylmetacrylate bone cement in percutaneous vertebroplasty: viscosity associated with cement leakage. *Spine* 2010. E1037-44.
21. Kasó G, Horváth Z, Szenohradszky K, Sándor J, Dóczi T. Comparison of CT characteristics of extravertebral cement leakages after vertebroplasty performed by different navigation and injection techniques. *Acta neurochirurgica* 2008. 677-83; discussion 83.
22. Anselmetti, Zoarski, Manca, et al. Percutaneous Vertebroplasty and Bone Cement Leakage: Clinical Experience with a New High-Viscosity Bone Cement and Delivery System for Vertebral Augmentation in Benign and Malignant Compression Fractures. *Cardiovascular and interventional radiology* 2008.
23. Bhatia C, Barzilay Y, Krishna M, Friesem T, Pollock R. Cement leakage in percutaneous vertebroplasty: effect of preinjection gelfoam embolization. *Spine* 2006. 915-9.
24. Hiwatashi A, Yoshiura T, Noguchi T, et al. Usefulness of cone-beam CT before and after percutaneous vertebroplasty. *AJR* 2008. 1401-5.
25. Lee IJ, Choi AL, Yie M-Y, et al. CT evaluation of local leakage of bone cement after percutaneous kyphoplasty and vertebroplasty. *Acta radiologica* 2010. 649-54.
26. Pitton MB, Drees P, Schneider J, et al. Evaluation of percutaneous vertebroplasty in osteoporotic vertebral fractures using a combination of CT fluoroscopy and conventional lateral fluoroscopy. RöFo : Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin 2004. 1005-12.
27. Groen RJM, du Toit DF, Phillips FM, et al. Anatomical and pathological considerations in percutaneous vertebroplasty and kyphoplasty: a reappraisal of the vertebral venous system. *Spine* 2004. 1465-71.
28. Bono CM, Heggeness M, Mick C, Resnick D, Watters WC. North American Spine Society: Newly released vertebroplasty randomized controlled trials: a tale of two trials. *Spine J* 2010. 238-40.
29. Klazen CA, Lohle PN, de Vries J, et al. Vertebroplasty versus conservative treatment in acute osteoporotic vertebral compression fractures (Vertos II): an open-label randomised trial. *Lancet* 2010.
30. Schmidt R, Cakir B, Mattes T, Wegener M, Puhl W, Richter M. Cement leakage during vertebroplasty: an underestimated problem? *Eur Spine J* 2005. 466-73.
31. Mousavi P, Roth S, Finkelstein J, Cheung G, Whyne C. Volumetric quantification of cement leakage following percutaneous vertebroplasty in metastatic and osteoporotic vertebrae. *J Neurosurg* 2003. 56-9.
32. Venmans A, Klazen CA, van Rooij WJ, de Vries J, Mali WP, Lohle PN. Postprocedural CT for perivertebral cement leakage in percutaneous vertebroplasty is not necessary-results from VERTOS II. *Neuroradiology* 2010.
33. Do HM, Kim BS, Marcellus ML, Curtis L, Marks MP. Prospective analysis of clinical outcomes after percutaneous vertebroplasty for painful osteoporotic vertebral body fractures. *AJNR* 2005. 1623-8.
34. Muijs S, Nieuwenhuijse M, Van Erkel A, Dijkstra P. Percutaneous vertebroplasty for the treatment of osteoporotic vertebral compression fractures: EVALUATION AFTER 36 MONTHS. *Journal of Bone and Joint Surgery - British Volume* 2009. 379.
35. Trout AT, Kallmes DF, Gray LA, et al. Evaluation of vertebroplasty with a validated outcome measure: the Roland-Morris Disability Questionnaire. *AJNR* 2005. 2652-7.
36. Mudano A, Bian J, Cope J, et al. Vertebroplasty and kyphoplasty are associated with an increased risk of secondary vertebral compression fractures: a population-based cohort study. *Osteoporosis international*.

37. Lim, Kim, Kim, Baek. Multiple cardiac perforations and pulmonary embolism caused by cement leakage after percutaneous vertebroplasty. European journal of cardio-thoracic surgery
38. Baroud G, Heini P, Nemes J, Bohner M, Ferguson S, Steffen T. Biomechanical explanation of adjacent fractures following vertebroplasty. Radiology 2003. 606-7; author reply 7-8.
40. Syed MI, Patel NA, Jan S, Harron MS, Morar K, Shaikh A. New symptomatic vertebral compression fractures within a year following vertebroplasty in osteoporotic women. AJNR 2005. 1601-4.