Vertebroplasty and Kyphoplasty

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Abstract

Vertebroplasty has had a major impact on the management of vertebral compression fractures of all etiologies in the past 20 years. A number of variations of the technique initially described by Deramond have been described, including kyphoplasty, lordoplasty, and device-implanting procedures, all of which appear to provide similar pain relief rates as vertebroplasty, commonly in the 90 % range. Although the effectiveness of vertebroplasty (and other vertebral augmentation procedures) has been challenged, there is *significant* evidence for its effectiveness. Given the economic pressures involved in health care, the effectiveness of any procedure will be scrutinized. Further analyses of vertebroplasty will most likely result in establishing the appropriateness, clinical effectiveness, and cost-effectiveness of vertebral augmentation.

1 Introduction

Although vertebral augmentation procedures are relatively recent, their therapeutic impact and benefit to patients has been measurable. Hervé Deramond, a French neuroradiologist, is credited with performing the first vertebroplasty in 1984 on a young woman with a destructive hemangioma of the dens axis causing intractable cervical pain and instability (Galibert et al. 1987). In that patient, percutaneous injection of acrylic cement in the vertebra both improved craniocervical stability and provided profound lasting pain relief. In the ensuing few years, Deramond and his group successfully applied the technique to the treatment of painful, osteoporosis-induced or cancer-related vertebral fractures, which resulted in rapid worldwide adoption of vertebroplasty (Grados et al. 2000). In the mid 1990s, the procedure was introduced in the United States by Lee Jensen and the University of Virginia group (Jensen et al. 1997).

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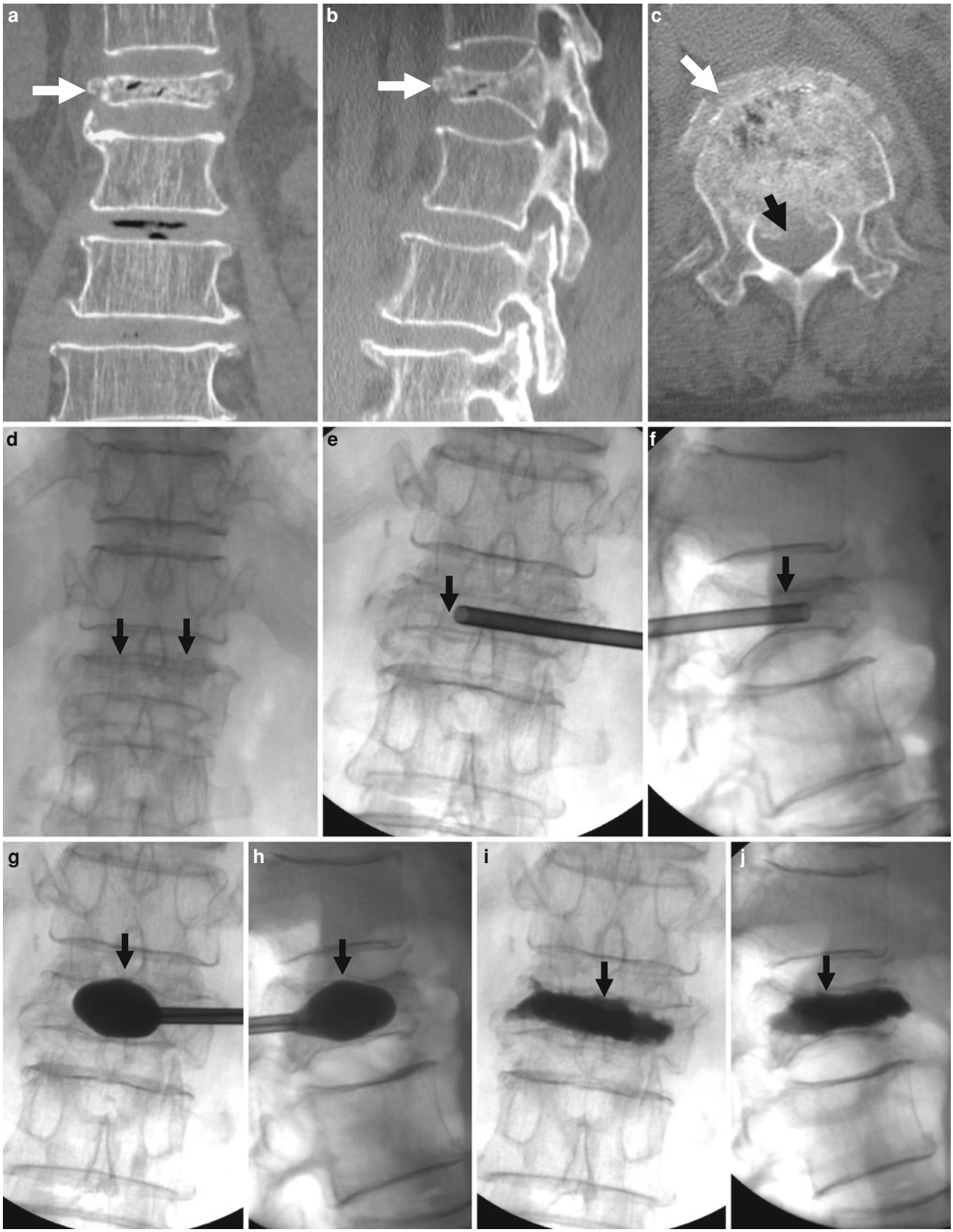
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◀ **Fig. 1** 85-year-old woman with severe back pain from L1 fracture with mild retropulsion. Unilateral transpedicular kyphoplasty results in pain relief. CT of the lumbar spine, coronal (**a**) and sagittal (**b**) reconstruction images show fracture of the L1 vertebra with vacuum phenomenon and severe height loss. Axial imaging (**c**) also confirms retropulsion. X-ray (**d**) shows 70 % height loss (arrows). Kyphoplasty trocar (*arrows*) has been introduced into the vertebral body of L1 through a right transpedicular approach visible on AP (**e**) and lateral (**f**) views. AP (**g**) and lateral (**h**) views show that single balloon (*arrow*) positioned in the center of the vertebral body provides significant height recovery. AP (**i**) and lateral (**j**) views show that moderate reduction has been obtained with cement injection (*arrows*). The posterior wall is not compromised

Vertebroplasty has made a major difference for patients with vertebral compression fractures, whether from cancer or osteoporosis, and has contributed in many instances to improved quality of life while decreasing, replacing, or delaying further pain and disability.

A number of variations on the initial procedure described by Deramond have been developed. Kyphoplasty, which uses a dilatation balloon to restore some degree of height to the treated vertebra and reduce angular kyphosis, was initially marketed as an improvement over vertebroplasty for the treatment of osteoporotic fractures (Lieberman et al. 2001). A number of other variations followed, most of which involve implantation in the vertebra of metallic or plastic devices (Kiva™, Optimesh®, StatXx-FX®) (Ortiz and Mathis 2010).

Despite recent controversy as to the effectiveness of vertebroplasty in pain relief, which was generated by two articles published in the same August 2009 issue of the *New England Journal of Medicine* (Kallmes et al. 2009; Buchbinder et al. 2009), there is strong evidence to support the role of vertebroplasty and other augmentation procedures in properly selected patients.

2 Patient Selection

Vertebral compression fractures are most commonly the result of osteoporosis. In addition, vertebral fractures are the most common osteoporosis-related fracture. Osteoporosis constitutes a significant burden to society, with more than 700,000 vertebral fractures in the United States per year and an annual cost estimated at several billion dollars (Riggs and Melton 1995). Although osteoporosis affects predominantly women in the post-menopausal period, men are almost as equally affected by standards of bone mass measurement.

While there is no single method for predicting which patients will be most at risk for fractures, some observations may be helpful. Siminoski et al. (2005) have pointed out that patients who lose significant height (4 cm or more) within a short period of time are very likely to have experienced a vertebral compression fracture. When a vertebral fracture occurs, there is a significant increase in load on muscles, ligaments, and facets, which can cause muscle spasms and precipitate facet arthropathy, triggering additional pain-generating mechanisms. The center of gravity is displaced forward with angular kyphosis, causing an increased risk of falls, and therefore an increased risk for additional axial and appendicular fractures.

The goals of treatment are pain relief, fracture reduction, and vertebral reconstruction.

Vertebral body fractures that are associated with compromise of the posterior wall and retropulsion, particularly if associated with neurological deficit, are traditionally considered best treated by conventional surgical techniques. However, percutaneous vertebral augmentation procedures may be performed successfully in selected cases (Fig. 1).

Extreme compression fractures (vertebra plana) make the procedure technically difficult, although not impossible if the endplates are intact (Fig. 2). Traumatic fractures not associated with osteoporosis that cause recurrent severe pain may be considered for vertebroplasty, particularly if relatively recent and if surgery is not a reasonable consideration (Fig. 3). Kyphoplasty has also been reported in the successful treatment of a vertebral fracture associated with Guillain-Barré syndrome, promoting significant improvement in functional activity and neurological function by allowing the patient to enroll immediately in a rehabilitation program (Masala et al. 2004).

3 Vertebroplasty, Kyphoplasty, and Newer Vertebral Augmentation Procedures

Vertebroplasty, the first vertebral augmentation procedure described, involved the direct injection of bone cement within the spongious bone of the vertebral body through needles inserted through one or both pedicles. The first variation of the technique was to use a unilateral transpedicular approach to increase the safety and decrease the duration of the procedure. Technical improvements to the vertebroplasty procedure soon took place, the most notable being curved and directional needles (Cook®, DePuy Osseon®, AvaFlex®), bone filler needles (CareFusion®, Stryker®), cavity creating devices (Latitude®), and newer cements with higher viscosity containing bioceramics (Cortoss®) or calcium phosphate hydroxyapatite (Actos®).

The concept of inserting and inflating a balloon into a vertebral body was first developed in the mid-1980s by an orthopedic surgeon, Dr. Mark Reiley and an engineer, Arie Scholten. It was not until 1994 that Dr. Reiley was able to find investors interested in his “balloons in bones” idea.

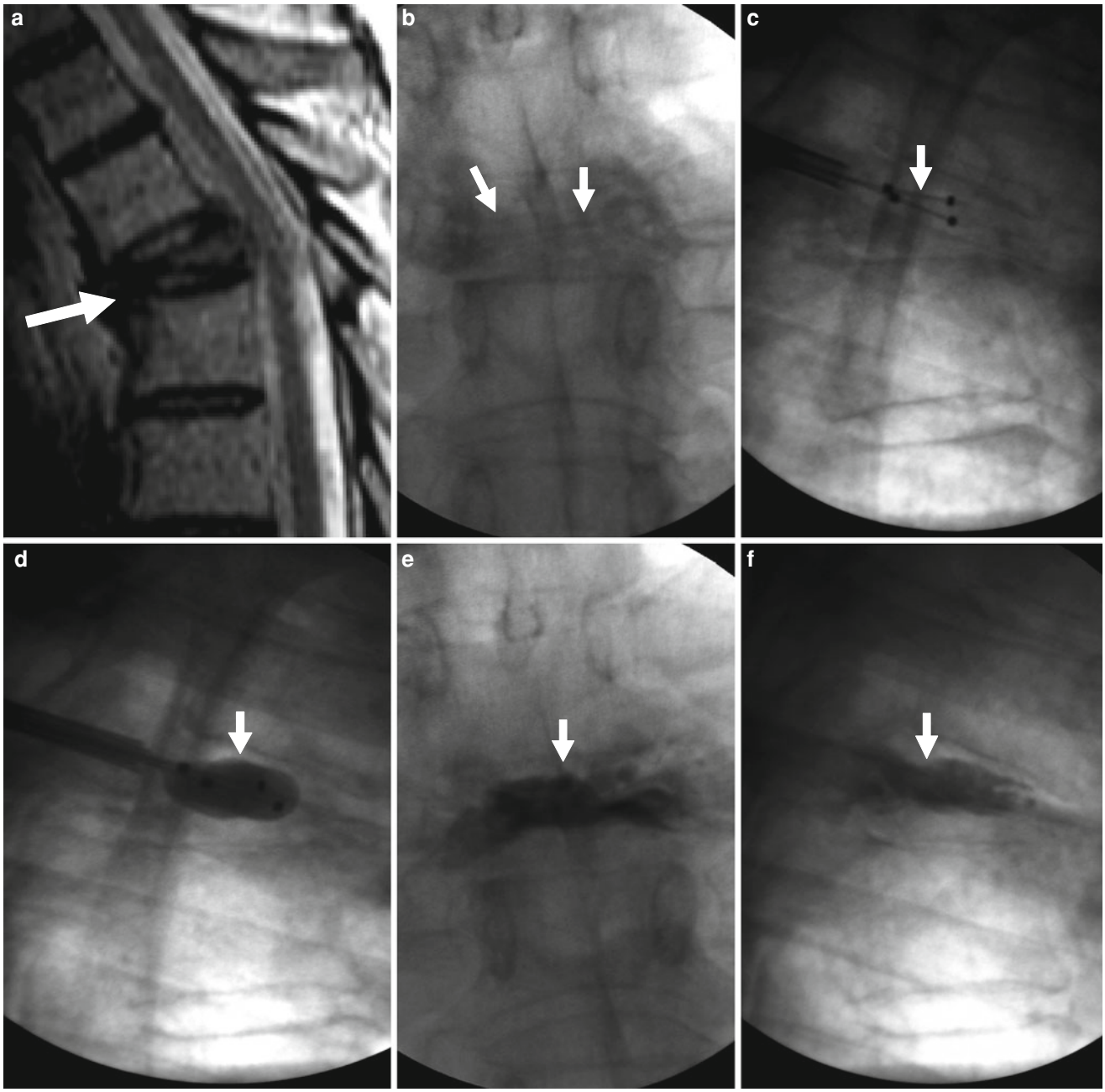


Fig. 2 Kyphoplasty for painful T5 vertebra plana fracture in a 67-year-old man with multiple myeloma. Excellent pain relief. **a** Sagittal T2 weighted MRI shows T5 fracture with severe anterior wedging and height loss (*arrow*) in a vertebra plana pattern. **b** X-ray, anteroposterior view shows severe height loss of T5 (*arrows*). **c** X-ray, lateral view shows deflated kyphoplasty balloons placed within the vertebral body of T5 (*arrow*). **d** X-ray, lateral view shows inflated kyphoplasty balloons within T5 (*arrow*). **e** X-ray, anteroposterior view shows excellent cement filling in T5 (*arrow*). **f** Lateral X-ray shows excellent reduction of T5 (*arrow*)

The newly formed Kyphon Corporation (Sunnyvale, CA) succeeded in developing a balloon capable of displacing bone. The KyphX® Inflatable Bone Tamp™ received 510(k) clearance from the United States Food and Drug Administration (FDA) in July 1998 (Fig. 4).

Lordoplasty is a variation of vertebroplasty which reportedly has similar pain relief rates (in the 90 % range), and has the theoretical advantage of reducing vertebral and segmental kyphosis by 10–15° (Orler et al. 2006). Lordoplasty uses cannulas in the fractured and adjacent verte-

brae, which function as internal fixators; a lordotic moment is applied via the cannulas, allowing reduction of the lordosis while the fractured vertebra is simultaneously filled with cement.

Vertebral body remodeling devices all differ from vertebroplasty, lordoplasty, or kyphoplasty as they involve the permanent implantation within the vertebral body of a device in addition to bone cement. Whether implantable devices have greater effectiveness and safety over vertebroplasty and kyphoplasty is not known at this time.

The Kiva™ device (Benvenue Medical Inc, Santa Clara, CA) is a polyether ether ketone (peek) implant (PEEK-OPTIMA®) which is advanced via a transpedicular approach through a Nitinol (nickel titanium) Kiva wire (Fig. 5). This device is currently being investigated in a multicenter trial, the KAST Study (Kiva™ System as a Vertebral Augmentation Treatment—A Safety and Effectiveness Trial).

The StaXx FX Structural Kyphoplasty System® (Spine Wave, Shelton, CT) is another remodeling device which consists of wafers implanted in the fractured vertebra via a percutaneous peripedicular approach and a wide-based inserting needle. StaXx wafers are made from polyether ether ketone and are 1 mm thick each. Wafers are inserted one at a time, using a wedge action to create vertical lift and reduce the fractured vertebral body. The first wafer, or base wafer, acts as a foundation for subsequently inserted wafers. Once all wafers are inserted, bone cement is injected into the vertebral body for further fixation and stabilization. A small volume of cement is also specifically injected anteriorly at the base of the wafer stack, securing the anterior column.

The Optimesh® device (Spineology, Saint-Paul, MN) is a surgical mesh made of polyethylene terephthalate (PET). The mesh pouch, which contains impacted granular bone graft, is inserted in its empty state through a small cannula and then packed in situ with bone graft once in place. As more bone graft material is added to the mesh, the gradually increasing volume deploys the OptiMesh® implant in its final geometric state and generates significant distractive force. When completely filled, the OptiMesh® implant fibers become taut and granular mechanics transforms the contained graft into a custom-fit, rigid, load-bearing graft pack. The Optimesh® device is radiolucent and compatible with all imaging modalities.

The VerteLift™ implant (SpineAlign Medical Inc, Pleasanton, CA) is a wire made of Nitinol alloy which comes in two basic shapes and a range of sizes. The device acts as an internal scaffold to engage the vertebral body endplates, while providing and maintaining lift until bone cement is injected. Prior to injection of bone cement, the VerteLift™ implant is fully retrievable. The VerteLift™ implant is currently approved in Europe, and undergoing investigational device exemption evaluation in the United States.

4 Indications and Contraindications

Currently accepted indications include painful vertebral compression fractures from (a) osteoporosis (primary or secondary), (b) neoplastic infiltration, (c) painful, "aggressive" vertebral hemangiomas, and (d) trauma when minimal displacement is present and surgery is contraindicated (Fig. 3).

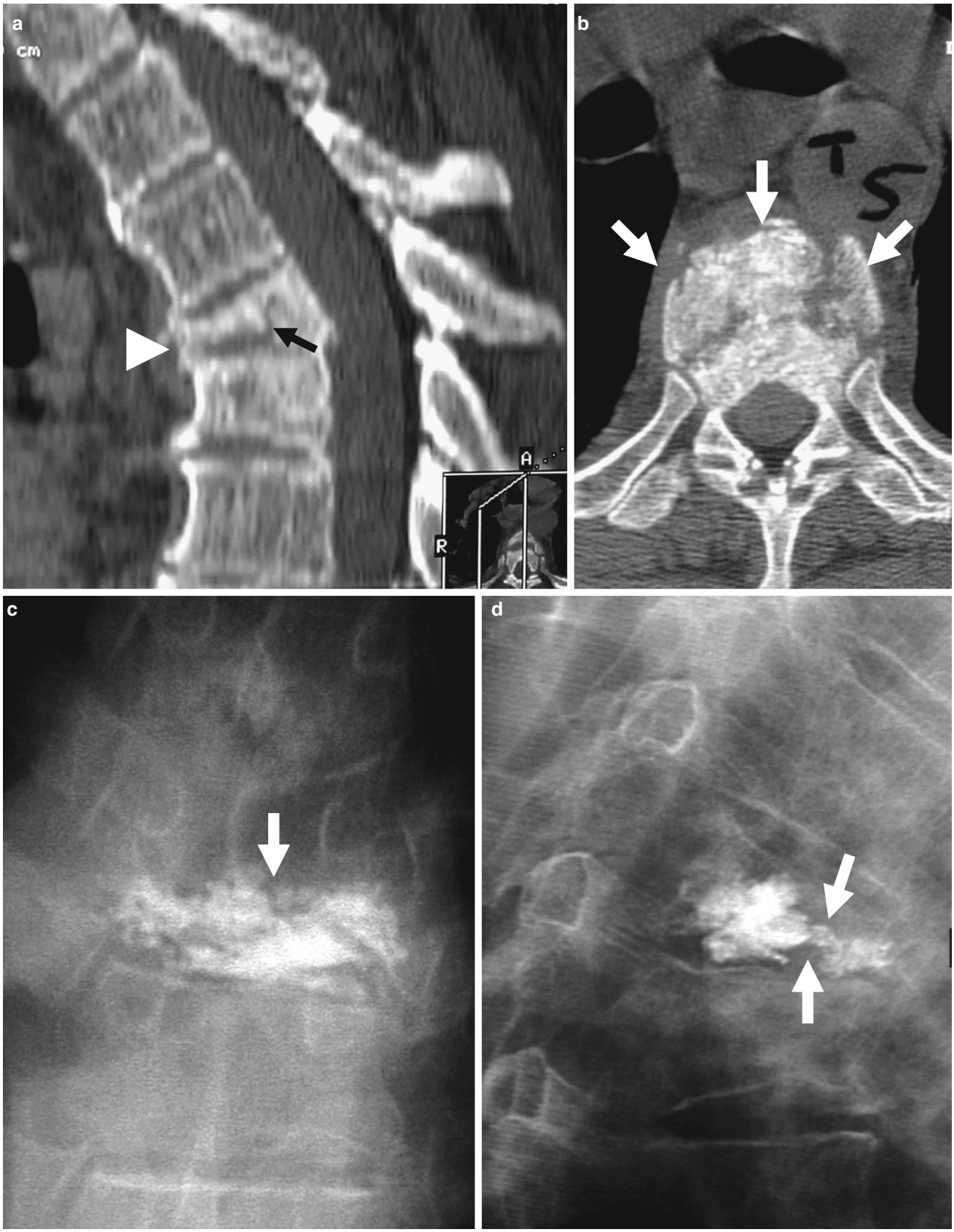
There are no absolute contraindications to vertebroplasty or other vertebral augmentation procedures. There are relative contraindications to vertebral augmentation procedures that include (1) the presence of a systemic infection, and (2) lack of appropriate surgical backup, which could delay treatment. Bleeding conditions are not considered a contraindication, as they can be adequately controlled in the majority of patients prior to the procedure.

5 Complications

All complications of vertebral augmentation procedures are relatively uncommon, particularly severe ones. In the early 1990s, the United States FDA initiated the Manufacturer and User Facility Device Experience (MAUDE), a nationwide database which was designed to record the details of medical complications occurring from the use of medical devices associated with indexed procedures. Recorded data consists of user facility reports from 1991, distributor reports from 1993, voluntary reports from June 1993, and manufacturer reports from August 1996.

The earliest reports concerning vertebroplasty and kyphoplasty original clinical reports were filed in 1999. In November 2004, the first FDA MAUDE report on complications resulting from the use of medical devices associated with vertebroplasty and kyphoplasty was published.

A total of 43 adverse events were reported out of approximately 190,000 procedures (0.02 %). Reported complications included 4 deaths, 21 instances of neurologic deficits related to cement canal intrusion or epidural hematoma (6 of which were permanent), 3 episodes of blood pressure drop, 2 pulmonary embolisms, 2 infections (1 diskitis, 1 osteomyelitis), 1 pneumothorax, and 11 technical reports of inconsequential equipment breakage. Twenty-five of the 43 events were major, including 4 deaths and 21 cord compressions requiring surgery, with 6 permanent neurologic injuries (Nussbaum et al. 2004). These data, however, likely underrepresent the actual complication rate from these procedures which is better reflected in clinical studies. Deaths were presumed and reported to occur as a result of reactions to the acrylic bone cement, the free polymer portion of which has known cardiotoxicity and can cause cardiac arrhythmias and hemodynamic instability (Kaufmann et al. 2002). As the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◀ **Fig. 3** Example of traumatic fracture in 66-year-old man treated with vertebroplasty with excellent pain relief. **a** Sagittal reconstruction of thoracic spine CT shows marked anterior wedging and height loss (*arrowhead*), and fracture line (*arrow*). **b** Axial imaging at T5 shows several fracture lines (*arrows*) in the vertebral body resulting in a "burst" pattern. **c** Anteroposterior view shows discontinuous cement deposition within the vertebral body (*arrow*). **d** Lateral view also shows irregular cement deposition in the vertebral body of T5, with apparent vertebral reconstruction and no posterior cement leakage (*arrows*)

risk is dose-dependent, this complication has only been reported when a large number of vertebrae were treated per session.

Neurologic compromise can occur from spinal cord compression because of leakage of large amounts of cement into the epidural venous plexus (Shapiro et al. 2003; Lee et al. 2002; Harrington 2001), requiring expedited surgical evacuation (Shapiro et al. 2003). Cement leakage may also cause direct nerve root compression which can cause new pain or exacerbation of pain (Lee et al. 2002).

Leaking cement in the paravertebral space surrounding the vertebral body usually does not lead to clinical complications, and may occur in as many as 10 % of procedures, (Coumans et al. 2003; Mathis et al. 2001) although transient dysphagia has been specifically reported at the cervical level from esophageal compression (Depriester et al. 1999). Leakage of cement into the intervertebral disk, especially in osteoporotic fractures with rupture of the inferior vertebral body endplate, may occur, without reported clinical consequences (Depriester et al. 1999). With vertebral puncture, there is also a risk of fracture, avoided by meticulous positioning with directed fluoroscopic technique (Pierot and Boulin 1999) or CT guidance in selected instances (Gangi et al. 1998).

With a posterolateral approach (Laredo et al. 1994), there is a risk of pneumothorax at the thoracic level, and of psoas hematoma at the lumbar level (Table 1).

6 Specific Issues with the Geriatric Population

In the elderly, a number of specific issues require special attention, including pre-treatment work-up, procedural technique, and follow-up.

6.1 Adequate Identification of Fractures

Compression fractures have been traditionally diagnosed on plain radiographs, which allow evaluation of bone structure, including the posterior vertebral body wall, and quantification of height loss when present. In the elderly population, several fractures of various ages may coexist, which can complicate identification of the symptomatic level on X-ray imaging alone, even if combined with fluoroscopic-guided provocative manual palpation and a reliable clinical examination. The age of a fracture is an important determinant of response to treatment, and plays an important role in treatment option selection, i.e. in considering the potential superiority of kyphoplasty or other augmentation procedures over vertebroplasty (Spiegl et al. 2009). Magnetic resonance imaging (MRI) is the mainstay of patient evaluation. It is very useful in dating a fracture, showing bone marrow edema in the early stages of a fracture that is not present in older fractures (Fig. 6) (Do 2000; Lindsay et al. 2001). In particular for patients with multiple myeloma, MRI has been shown to be superior to bone scintigraphy (Masala et al. 2005).

The work-up of metastatic spinal lesions also heavily relies on MRI which allows objective and reproducible quantitative assessment of the degree of compression, epidural extension, paraspinal extension, presence of other lesions, and the degree of vascularity (Georgy 2008).

A special mention must be made of SPECT/CT (single photon emission computed tomography/X-ray computed tomography), a relatively new hybrid application which combines metabolic information from SPECT images with accurate anatomical information from CT. This technique may be particularly useful in older patients with multiple fractures and severe claustrophobia, pacemaker, or other contraindication to MRI (Suárez et al 2009; Sudhakar et al. 2010) (Fig. 7).

6.2 Analgesia

Elderly patients who present for the evaluation and treatment of a vertebral compression fracture are often on narcotic pain medications for chronic pain from various causes, and their medication dependency may be exacerbated by the presence of a compression fracture. These patients commonly have a higher response threshold than average, for which higher doses of sedation are typically required during a procedure, and often they suffer from some degree of confusion. In anticipation of a procedure in such patients, it is helpful to reduce the oral intake of narcotics and attempt substituting anti-inflammatory drugs, i.e. ibuprofen or ketorolac (Toradol®), to better control intraprocedural sedation.

6.3 Patient Positioning

Elderly patients have a high incidence of spondylosis, arthritis, and advanced osteoporosis.

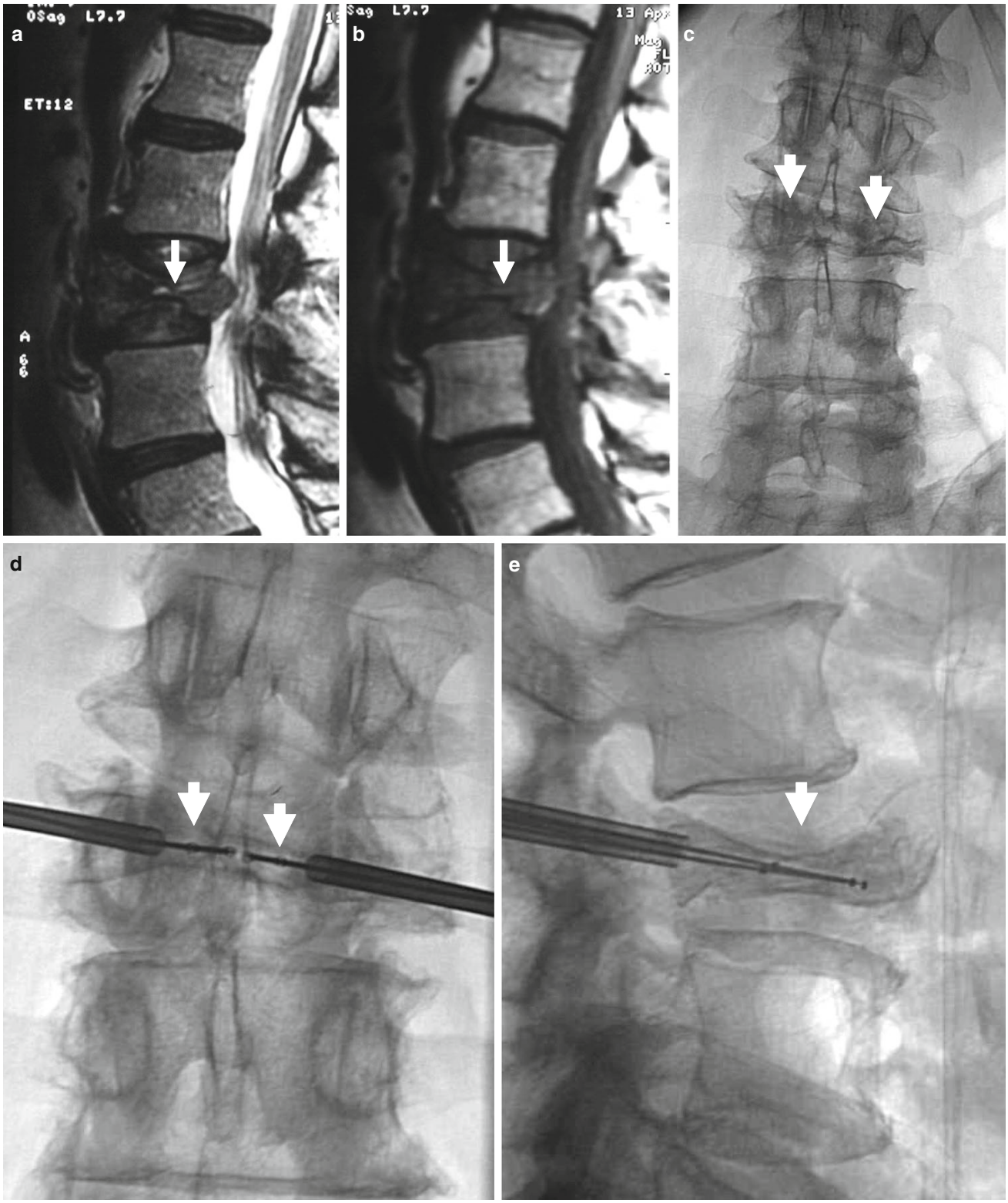
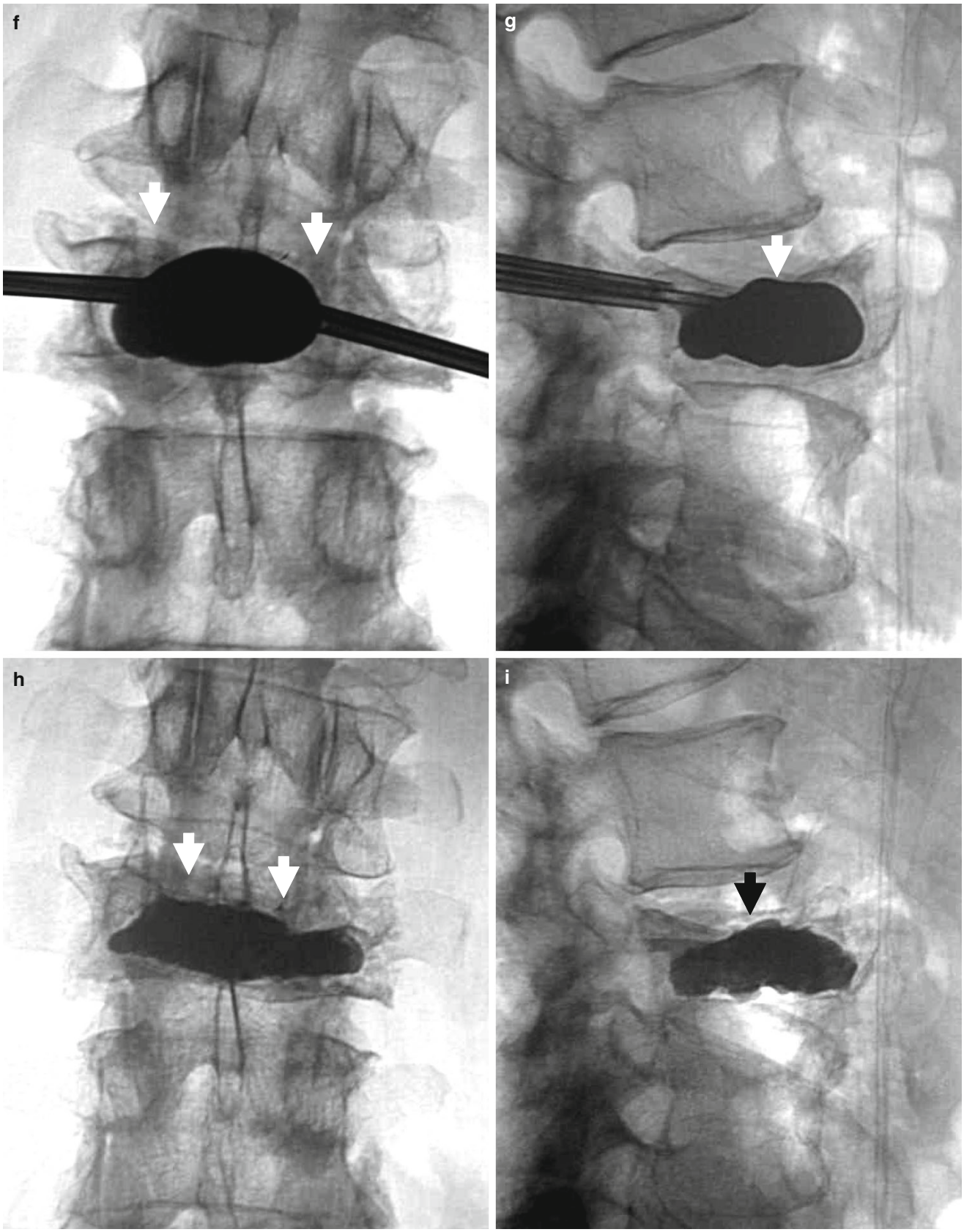


Fig. 4 Kyphoplasty using a bilateral transpedicular approach to treat an extremely painful fracture of L3 with significant retropulsion in a 75-year-old woman with scoliosis. **a** Sagittal T2 weighted MRI shows a hyperintense horizontal cleft in the superior aspect of the vertebral body of L3 (*arrow*). **b** Sagittal T1 weighted MRI shows hypointense signal within the cleft (*arrow*), confirming bone marrow edema. **c** X-ray of lumbar spine shows L3 fracture with 70 % height loss (*arrows*). **d**, **e**. Excellent placement of kyphoplasty balloons within L3 vertebral body (*arrows*). Note some degree of reduction of scoliosis. **f**, **g** Balloon inflation results in approximately 50 % height recovery (*arrows*). **h**, **i** After cement filling, there is approximately 30–40 % height recovery (*arrows*) with fracture reduction, and less pronounced scoliosis



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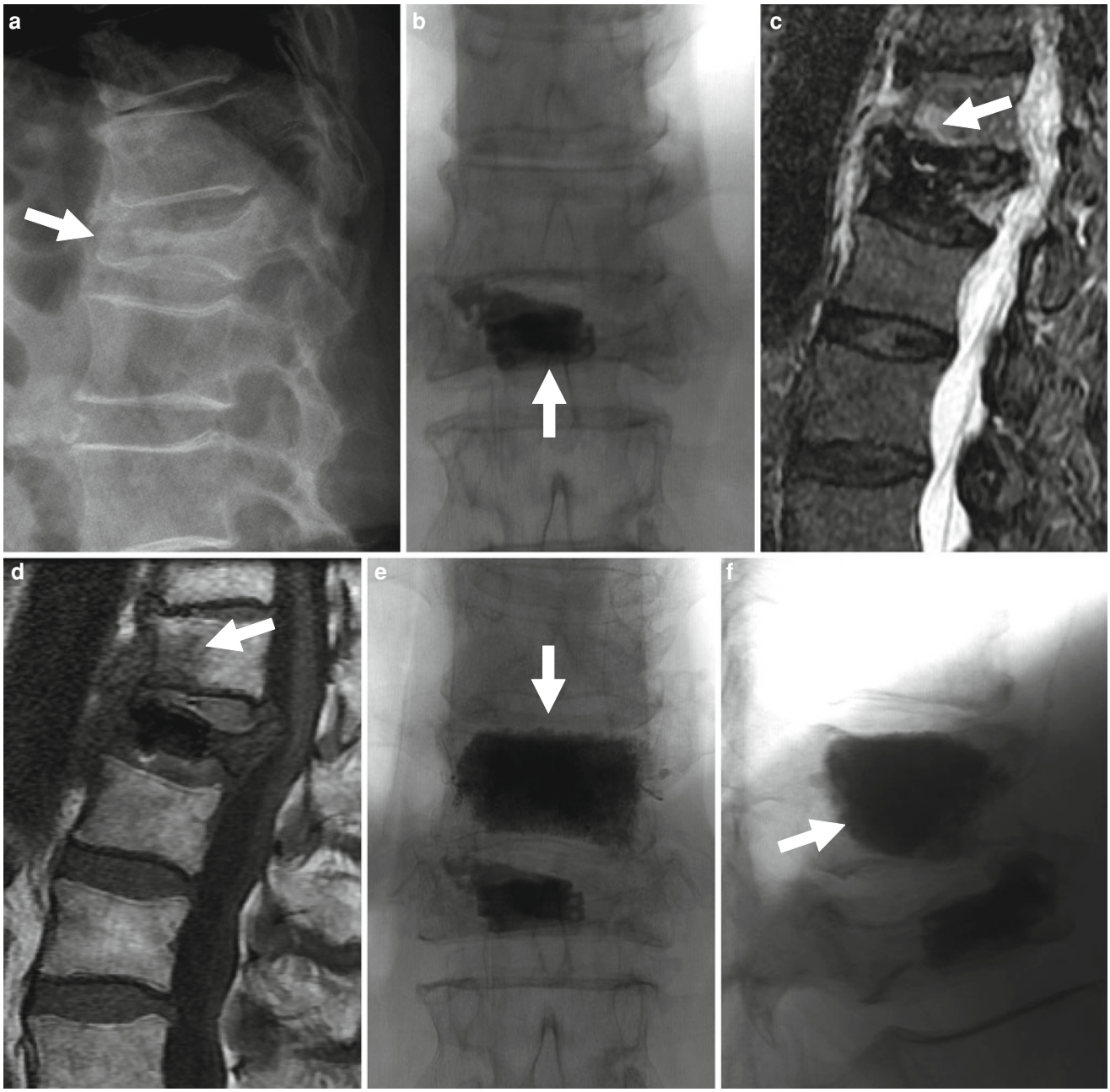

Fig. 5 72-year-old woman with painful L1 fracture treated with the Kiva™ device. Recurrent pain is caused by a fracture at T12, subsequently treated with vertebroplasty. **a** Thoraco-lumbar spine X-ray shows a fracture at L1 with 70 % height loss and moderate retropulsion (*arrow*). **b** Antero-posterior view of the lumbar spine shows the Kiva device and a small amount of bone cement within the vertebral body of L1 (*arrow*). T2-weighted (**c**) and T1-weighted (**d**) MRI shows bone marrow edema in fractured T12 vertebral body (*arrows*). Following vertebroplasty, AP (**e**) and lateral views (**f**) show diffuse and even filling of the T12 vertebral body (*arrows*). Pain relief was immediate

Careful and methodical positioning is particularly important in order to avoid causing new pathology, especially as osteoporosis results in challenging fluoroscopic visualization of bony structures. Rib fractures may occur relatively easily in these patients as a result of suboptimal positioning on the X-ray table, or from pressure on the ribcage from needle insertion through the pedicles. Particular attention should be directed to supplemental padding of contact points. Muscle spasms may also appear after such procedures and can be exacerbated by positioning maneuvers. Patients with a high level of confusion may be at risk for falling off the fluoroscopic table and therefore need to be closely monitored.

Table 1 Complications of vertebral augmentation procedures

Severe
Canal intrusion/epidural hematoma with permanent neurological damage
Infection (diskitis, osteomyelitis)
Pulmonary embolism
Myocardial infarction
Death
Moderate
Canal intrusion/epidural hematoma with transient neurological damage
Reactions to the acrylic (polymethylmethacrylate) bone cement -> cardiotoxicity, cardiac arrhythmias, and hemodynamic instability
Pneumothorax
Intraprocedural blood pressure drop
Minor
Uneventful equipment failure
Rib fractures
Transient post-kyphoplasty radicular pain

6.4 Procedural Sedation

Elderly patients may have significant age-related decreases in drug clearance, resulting in higher bioavailability of narcotic or other drugs taken at home prior to a procedure. In addition, renal and hepatic clearance of intravenous drugs may be significantly prolonged from age-related diminished enzyme activity, and in this patient population these complicating factors may not be accurately predicted from serum levels of creatinine and liver function tests. Particular care must be taken when midazolam is used for sedation, as a sudden drop in oxygenation may occur: severe drops in oxygen saturation levels may require emergent administration of a reversal agent. It is generally advisable to use as little sedation as possible in these patients, which emphasizes again the need for adequate patient preparation and education prior to the procedure (Luginbühl 2008).

6.5 Post-Procedural Care

Following procedures, elderly patients should be kept in observation for a reasonable and adequate amount of time which should cover a significant part of the half-life clearance of most drugs used. Even if spectacular pain relief results from the procedure, patients should be advised to be cautious when initially standing up and walking for a while following the procedure, as they remain at increased risk for falls. The effects of the procedure should be carefully monitored, as ancillary causes of pain may persist in these patients, i.e. facet disease, muscle spasm, undiagnosed, or new fractures, which may delay patient mobility, and may require intervention.

7 Effectiveness of Vertebral Augmentation Procedures

The first large-scale study to demonstrate the efficacy of pain relief with vertebroplasty in the United States is attributed to Jensen et al. (1997) who, in 1997, reported on 29 patients with painful osteoporotic vertebral fractures in whom a 90 % pain relief rate was obtained. This study played an important role in establishing vertebroplasty in the United States for the treatment of osteoporotic or neoplastic vertebral fractures. In 2000, a retrospective study by Barr et al. (2000) revealed that 95 % of 47 patients treated with vertebroplasty reported pain relief that was at least moderate.

Although an early metaanalysis of retrospective case series and uncontrolled studies reported rates of significant pain relief in the 70–80 % range in patients treated for a variety of osteolytic lesions including metastases, hemangiomas, multiple myeloma, and osteoporotic compression fractures, it was also noted that the durable positive response persisted for several months to several years after treatment (Levine et al. 2000). Later, larger scale meta analyses reported rates of pain relief for both vertebroplasty and kyphoplasty in the 90 % range (McGraw et al. 2002; Heini et al. 2000). McGraw et al. (2002) reported a series of 100 osteoporotic vertebral fractures treated with vertebroplasty, with a 97 % rate of significant pain relief at 24 h after treatment, and a 93 % rate of durable relief persisting at least 1 year (mean follow-up, 21.5 months). Similar data were demonstrated with kyphoplasty, with some authors reporting pain relief in 96.9 % of patients treated for osteoporotic fractures, mostly occurring within 24 h (Lane et al. 2000).

For neoplastic vertebral fractures, Weil et al. (1996) reported the first series of 37 patients with metastatic spinal fractures (20 men, 17 women; aged 33–86 years) treated successfully with vertebroplasty, and noted significant pain relief and increased stability in 73 %, with durable gains at 6 months. Later, Fourney et al. (2003) reported on 56 patients with cancer treated with vertebroplasty and kyphoplasty in whom complete pain relief was noted at a rate of 84 %, with persistent gains at 1 year.

A very interesting study is a retrospective evaluation of some of the earliest patients treated with vertebroplasty by the French group that described the original procedure (Deramond et al.) (Franc et al. 2010). Eighteen patients, treated between 1989 and 1998 for vertebral fractures due to osteoporosis ($n = 8$), hemangiomas ($n = 8$), and multiple myeloma ($n = 2$) were re-evaluated clinically and radiologically in 2007, nearly 20 years after their initial procedure. All patients experienced long-term pain relief and none demonstrated instability or disc degeneration disproportionate to that at adjacent vertebral levels (Franc et al. 2010). Similar pain relief rates are consistently reported for vertebroplasty

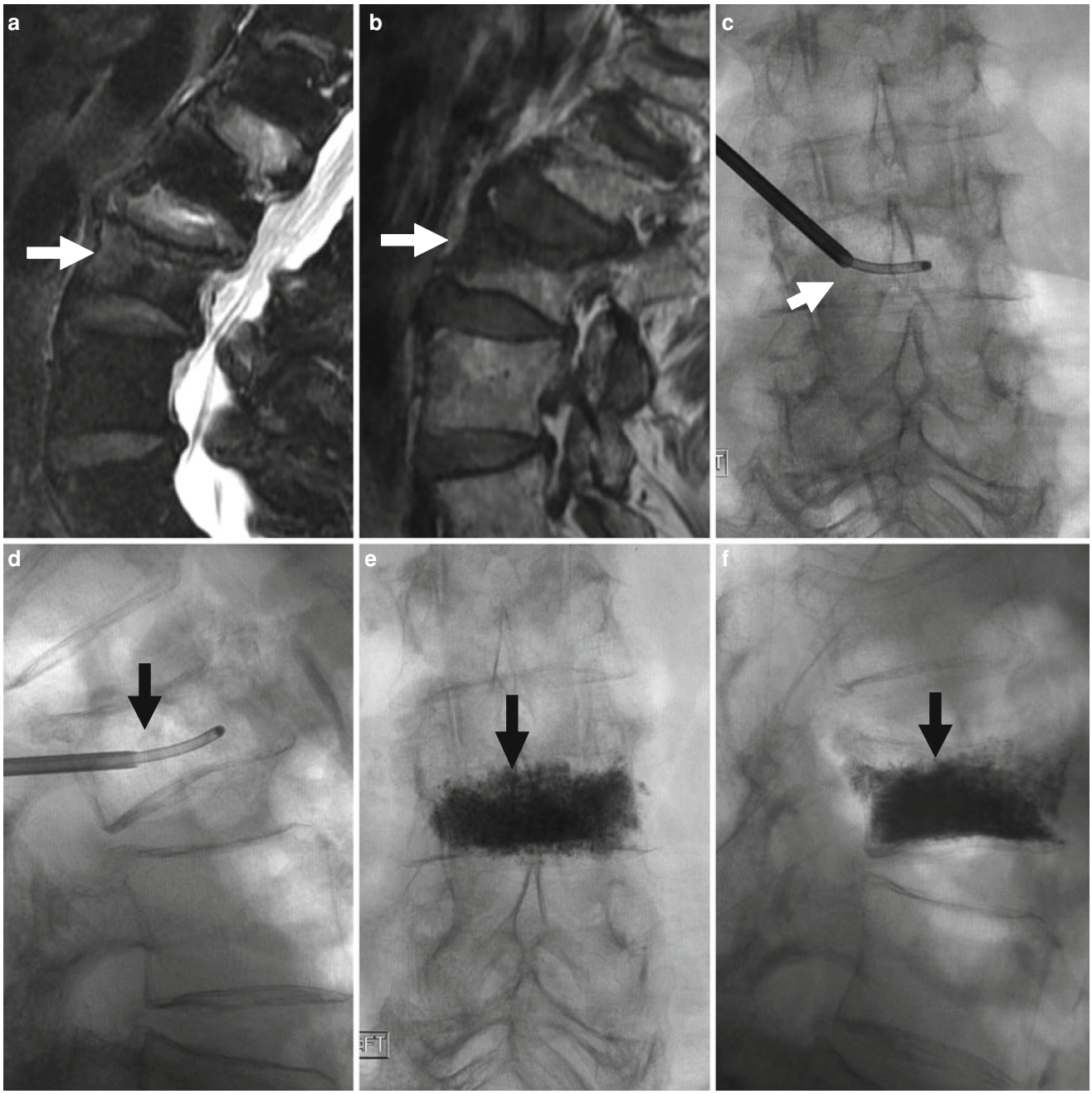

Fig. 6 86-year-old woman with very painful L3 fracture. Unilateral transpedicular vertebroplasty using an 11G curved needle. MRI, T2 (**a**), and T1 (**b**) weighted sagittal imaging shows diffused edema in the superior and anterior vertebral body of L3 (*arrows*). X-rays AP (**c**) and lateral (**d**) views show placement of the curved needle within the vertebral body (*arrows*). X-ray AP (**e**) and lateral (**f**) views show cement diffusely and evenly filling the L3 vertebral body (*arrows*), resulting in excellent pain relief

and kyphoplasty (Fourney et al. 2003; Wardlaw et al. 2009; Boonen et al. 2011; Lieberman and Reinhardt 2003; Ledlie and Renfro 2003; Lane et al. 2000).

Although kyphoplasty was initially marketed for the treatment of osteoporotic fractures as an improvement over vertebroplasty, by increasing vertebral height and reducing angular kyphosis, the overall comparative experience shows an average reduction of 4 mm for kyphoplasty versus 2.2 mm for vertebroplasty (Nussbaum et al. 2004). As yet, there is no indication as to whether the overall minimal difference in reduction is clinically significant. Another theoretical advantage of kyphoplasty is that "lower

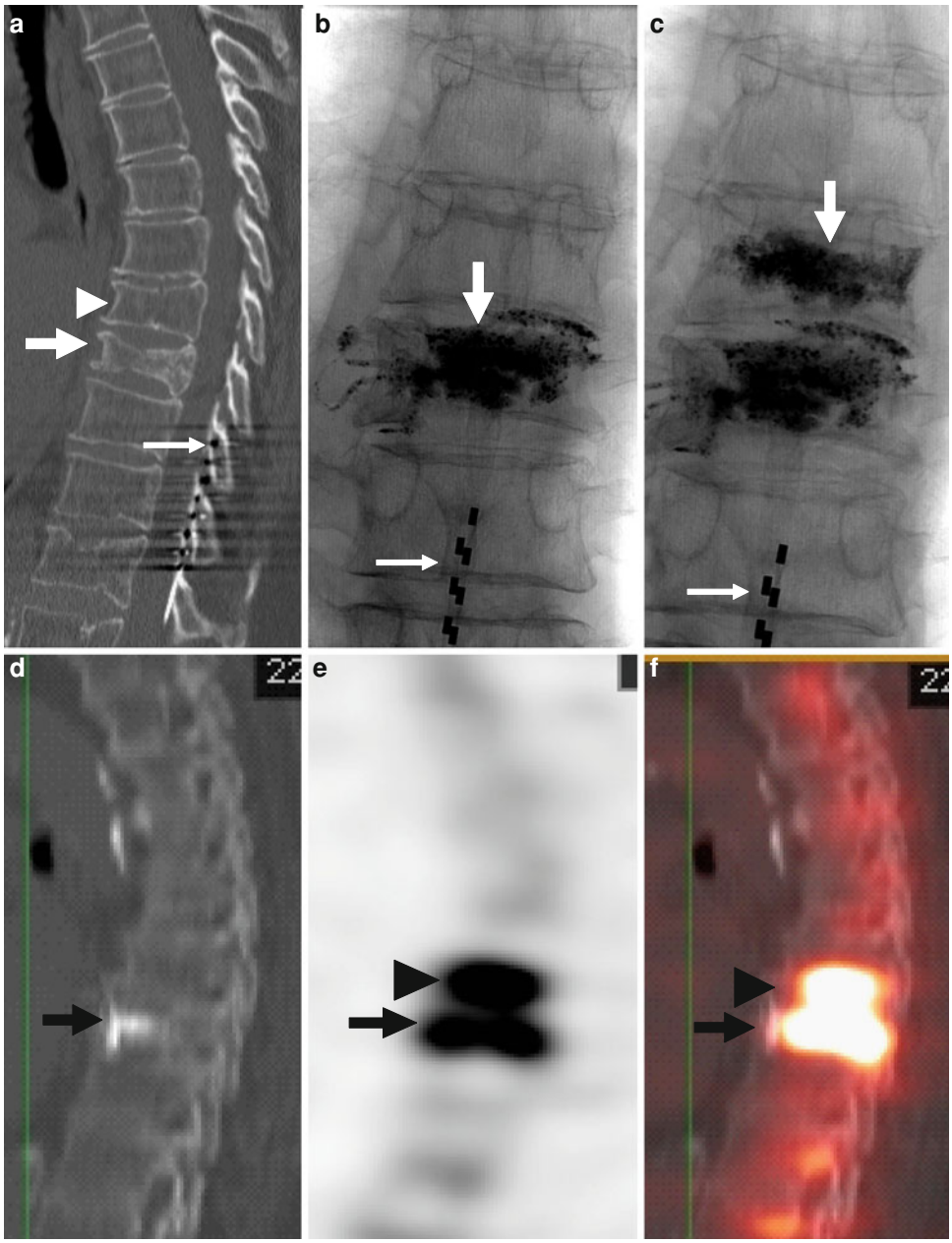

Fig. 7 80-year-old woman with atrial fibrillation and a pacemaker. Severe back pain is evaluated by CT which shows a fracture of the T8 vertebral body. Severe residual pain is assessed with SPECT/CT which shows a fracture at T7. Repeat vertebroplasty at this level results in pain relief. **a** CT of the thoracic spine, sagittal reconstruction shows a fracture of T8 (*arrow*). Mild irregularity of T7 is also present (*arrowhead*). Note spinal cord stimulator (*thin long arrow*). **b** X-ray of the thoracic spine, AP view, shows cement in the T8 vertebral body. Note spinal cord stimulator (*thin long arrow*). **c** X-ray of the thoracic spine, AP view, shows cement in T7 and T8. Note spinal cord stimulator (*thin long arrow*). **d**, **e**, **f** SPECT/CT shows significant uptake of Tc-199 m not only in the vertebral body of recently treated T8 (*arrow*), but also in the T7 vertebral body (*arrowhead*)

pressure" injections of cement are performed because a cavity is initially created in the vertebral body by the balloon tamp, rather than by injecting a "thinner" mixture as a forced intramedullary perfusate. Although one study found that there are more leaks with vertebroplasty than with kyphoplasty (Lieberman and Reinhardt 2003), another reported experimental evidence that higher pressures within voids created by bone tamps were noted with the use of larger systems (Agris et al. 2003).

With newer devices, pain relief rates seem to be consistent with the expected results from vertebroplasty and kyphoplasty. However, no large-scale data on outcomes are currently available.

8 Follow-Up and Risk of Subsequent Fractures

Patients should continue to be assessed after any vertebral augmentation procedure, particularly elderly patients. Some patients may have persistent pain despite adequate treatment. One reason for persistent pain may be incomplete treatment of the fractured vertebra, which might respond to a repeat procedure at the same level to obtain a more complete filling with cement (Kim et al. 2010). Another reason for persistent pain may be confounding facet joint pain: posterior facet instability and overload resulting from

a wedge fracture has been identified as a significant cause of pain in as many as one-third of patients, particularly elderly patients (Wilson et al. 2011). Still, the most common reason for recurrent or persistent pain following vertebral augmentation procedures is the presence of another undiagnosed vertebral fracture, or a new fracture.

An increased risk of new fractures involving vertebrae adjacent to previously treated ones has been suggested (Uppin et al. 2003; Fribourg et al. 2004). It has been estimated that this risk is 12.4 % following vertebroplasty, and that 67 % of new fractures occur in vertebrae that are immediately adjacent to the treated vertebra (Uppin et al. 2003). Part of the concern is that reinforced vertebral bodies may alter the biomechanics of the spine and contribute to adjoining fractures. Following kyphoplasty, an early study of 40 patients reported that 26 % of those treated developed a new fracture within 8 months (Fribourg et al. 2004), while a larger, later study found an overall incidence of a new fracture of 22.6 % per patient and 15.1 % per kyphoplasty procedure (Harrop et al. 2004).

Two large studies from recognized and experienced groups provided conflicting conclusions regarding the effects on adjoining vertebral fractures. Grados et al. (2000) found a slight but statistically significant increased risk of vertebral fracture adjacent to cemented vertebrae (odds ratio 2.27, 95 % CI 1.1-4.56), with an odds ratio of a vertebral fracture adjacent to an uncemented fractured vertebra of 1.44 (0.82–2.55). On the other hand, Jensen et al. (Jensen and Dion 2000) suggested that there may be no increased risk of a new fracture in adjacent vertebrae following vertebroplasty.

A biomechanical study of a small number of spine segments, some healthy, some treated with vertebroplasty, aimed to assess unconstrained axial compression with shear forces and torque minimized using a robotic arm. The authors concluded that new adjoining vertebral fractures were significantly more likely to result following vertebroplasty, due to the mechanism of endplate deflection (Fahim et al. 2011). A recent study of 794 patients divided equally between those with prior vertebroplasty and those with no vertebral augmentation procedure found a similar incidence of new fractures in each group (Chosa et al. 2011).

It is conceptually possible that new fractures may be precipitated by a bone-strengthening, spine-straightening, vertebral augmentation procedure, but it is also clear that, because of the diffuse nature of osteoporosis and metastatic cancer, new fractures are to be expected as part of the natural course of the disease. This is particularly true in the elderly population. As a result, it is necessary and appropriate to carefully follow those patients, and to be prepared to offer treatment for new fractures.

9 Current Controversy

Recently, the efficacy of vertebroplasty in obtaining pain relief has been seriously challenged by two randomized controlled trials or critical reports, which were published in the same 2009 issue of the *New England Journal of Medicine* (*NEJM*) (Kallmes et al. 2009; Buchbinder et al. 2009) Although concerns were expressed about both the conduct and the conclusions of those two studies, these concerns did not receive the same degree of media attention as the studies themselves.

9.1 Concerns with the Critical Reports

One concern with the critical reports concerns offering sham or simulated procedures to patients in severe pain. In both *NEJM* studies (Kallmes et al. 2009; Buchbinder et al. 2009), patients with fractures were treated with either vertebroplasty or a simulated procedure, consisting of intravertebral placement of a needle alone. While in the study by Kallmes et al. (2009) the amount of cement injected into the vertebral bodies is not specified, it can be inferred that volumes similar to standard clinical practice were used. On the other hand, in the study by Buchbinder et al. (2009) only minimal amounts of cement (3 mls) were injected in the vertebrae of the 38/78 patients treated. Because this study does not specify which levels were treated, it has been rightly pointed out that the most commonly fractured vertebrae, i.e., T10 through L3, were most likely the treated ones (Noonan 2009). In these levels, such a small volume of cement is often considered a low volume, and may not be as effective at restoring vertebral body structure and axial integrity and providing pain relief as larger volumes (Noonan 2009).

In the study by Kallmes et al. (2009), 63 % of patients who received the sham procedure correctly guessed the type of procedure by 14 days, as opposed to 51 % in the treated group. In this study, patients were promised the right to have the other procedure if pain relief was not adequate, provided they wait at least 1 month after the initial intervention. Of the patients who had received the sham procedure, 43 % chose to "cross over" to a vertebroplasty procedure, while only 12 % of the vertebroplasty patients chose to cross over in the opposite direction (Kallmes et al. 2009). Such differences have been construed as indicating lack of confidence in the sham procedure on the part of patients (Noonan 2009).).

9.2 Concerns with the Timing of Treatment

Concern has been raised regarding the time window of patient enrollment in both studies, in which patients with

back pain were treated within 12 months of their fracture. It is thought that patients with recent fractures of less than 8 weeks duration with unrelenting pain are most likely to benefit from vertebroplasty (Gangi and Clark 2010).).

9.3 Concerns with the Patient Population

In both critical reports the treated patients were outpatients. Prospective investigative evaluation of vertebroplasty may best be served by closely observing the pain syndrome in this patient population, rather than leaving such patients at home with potentially disabling pain which confines them to bed rest and narcotic analgesia. These patients are the most at risk for worsening of osteoporosis and other complications of bed rest and chronic narcotic intake. In the United States, by current Medicare standards, such patients would be considered candidates for vertebral augmentation on the basis of failure of conservative therapy. Of note, over half of the patients treated in the United States are admitted to hospitals for treatment of intractable pain, as indicated by the AMA resource-based data manager (2009 and 2010 data). This population is at high risk for hospital-associated morbidity (including nosocomial infections), additional bone loss, and increased costs for the hospital stay and pain control. Despite concerns regarding such a trial, it has been suggested that a randomized, prospective, double-blind study of hospital-bound patients with acute, painful osteoporotic vertebral fractures treated with vertebroplasty versus medical therapy would likely provide useful information regarding appropriately aggressive treatment (Wagner 2005)

9.4 Concerns with Evaluating the Effects of Treatment

In the study by Kallmes et al. (2009), a 30 % decrease in pain at 1 month was considered clinically meaningful pain relief. This study also reported a trend toward a higher rate of clinically meaningful improvement in pain in the vertebroplasty group when compared with controls (64 vs. 48 %), and concluded that vertebroplasty and simulated procedures produce "similar" effects. Similarly, in the study by Buchbinder et al. (2009) patient response was measured by using a 7-point ordinal scale, ranging from "a great deal worse" to "a great deal better." At 1 month, 34 % of the patients having undergone vertebroplasty classified their pain as "moderately better" or "a great deal better" versus 24 % of control patients, when compared with the stated conclusion that vertebroplasty and the sham procedure were essentially equivalent. An additional point for consideration is the expected statistical response to supposed minor differences between groups. The recommendation of the US FDA for clinical trials that show small effect sizes is to examine the cumulative distribution function of responses between treatment groups to characterize the treatment effect (U.S. Department of Health and Human Services, Food and Drug Administration 2009). Therefore, reductions in pain of 30 % should be considered as clinically meaningful responses, having previously been shown to reflect improved pain by pooling of response data from many studies (Georgy 2011). For endpoints such as pain level, clinical trials typically seek to show not only a statistically significant improvement in the primary efficacy endpoint, but also that the magnitude of the effect is clinically relevant (Snapinn and Jiang 2007). The "responder analysis" statistical approach is particularly well suited for such purposes, as it allows clear separation of "responders" and "non-responders" to a continuous primary efficacy measure (Snapinn and Jiang 2007). It has been appropriately argued that, although both the studies by Kallmes and Buchbinder did conduct a "responder analysis", neither was powered to detect differences by using this approach (Georgy 2011).

A large responder analysis performed by the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) Group has shown that patients treated with vertebroplasty were overall 35 % more likely than control subjects to experience a clinically meaningful reduction in pain at 1 month (Dworkin et al. 2008).

The results of a large study, the Vertebroplasty versus Conservative Treatment in Acute Osteoporotic Vertebral Compression Fractures (VERTOS) II trial were published following the two *NEJM* studies (Klazen et al. 2010). VERTOS was a prospective randomized trial of vertebroplasty and conservative treatment for 202 patients and showed that vertebroplasty resulted in greater pain relief than conservative treatment with a significant difference in mean visual analog scale (VAS) score between baseline and 1 month. The study concluded that in a subgroup of patients with acute osteoporotic vertebral compression fractures and persistent pain, percutaneous vertebroplasty is both effective and safe, and provides pain relief which is immediate, sustained for at least 1 year, and significantly exceeds the relief achieved with conservative treatment at an acceptable cost. This study did not receive the same level of media and insurance carrier attention given to the *NEJM* articles (Klazen et al. 2010).

Not surprisingly, following the publication of the two critical *NEJM* reports, proposals to deny coverage decision and reimbursement of both percutaneous vertebroplasty and percutaneous vertebral augmentation for their previously approved indications have been advanced by large counseling and authoritative bodies, such as the Noridian Administrative Services, a Medicare intermediary for 11 United States Western states, and the Ontario Health Technology Advisory Committee in Ontario, Canada (Georgy 2011). Whether

vertebroplasty and other augmentation procedures will continue to be covered remains to be seen.

10 Cost Considerations

Kyphoplasty and procedures that use remodeling devices cost more than vertebroplasty. For kyphoplasty, balloons and bone filler needles add expense to the procedure. In 2007, the cost of a KyphoPak kit (Kyphon) for a single-level vertebroplasty was $3423 as opposed to a few hundred dollars for vertebroplasty. Newer implantable devices will also incur costs that are higher than simple vertebroplasty. One study projects treatment costs at the current treatment rate of one in seven of the 700,000 fractures diagnosed each year in the United States. If kyphoplasty alone is used, treatment costs would add a global cost of $600 million (Nussbaum et al. 2004). In addition to the materials, fluoroscopy time and physician time are typically longer with newer, more complex procedures than vertebroplasty. It is likely that comparative effectiveness studies will be carried out to assess address and issues of cost.

11 Conclusion

Vertebroplasty has had a major impact on the management of vertebral compression fractures, by turning a potentially disabling and relatively common condition into an easily curable one. Whether technological improvements to the original procedure will translate into greater safety and effectiveness has yet to be established. Current concerns about the effectiveness of vertebral augmentation will need to be addressed as data continues to be collected. Improvements in technology may well include semi automated procedures using robotics and stereotactic guidance. Whether the cost and safety profile of the procedure and advances in our understanding of the epidemiology of osteoporosis and spine biomechanics will result in a potential prophylactic role for vertebral augmentation procedures in the future remains yet to be determined.

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