

MINIMALLY INVASIVE (PERCUTANEOUS) TREATMENT OF METASTATIC SPINAL AND EXTRASPINAL DISEASE – A REVIEW

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SUMMARY – Metastatic tumors are the most common malignancy of bone. Many patients with spinal metastases present with pain and pathologic fractures. The advent of interventional radiology resulted in alternative and less invasive treatment of these patients. This article presents minimally invasive (percutaneous) procedures that are currently in use, i.e. vertebroplasty, kyphoplasty, osteoplasty, radiofrequency ablation, cryoablation, and transarterial embolization. Indications, contraindications, results and complications are also discussed. According to our current knowledge of the results reported in the literature, minimally invasive techniques are successful methods for the treatment of metastatic spinal and extraspinal disease and can be used as alternative treatment to standard surgical or non-surgical procedures.

Key words: *Bone neoplasms – secondary; Spinal neoplasms – secondary; Vertebroplasty – methods; Kyphoplasty; Ablation techniques; Cryosurgery; Transarterial chemoembolization; Palliative care*

Introduction

Metastatic tumors are the most common malignancy of bone, affecting 10%-30% of all cancer patients¹. Vertebral column is the most common site of such metastases, spinal metastases being found in 36% of patients who died from neoplastic disease². Prostate, breast, lung, kidney, and thyroid cancers account for 80% of skeletal metastases^{1,2}. Due to medical advancement, there has been an increase in survival rates among cancer patients despite the increase in the incidence of metastatic lesions³. The predominant symptom in patients with spinal metastases is pain, which can be of three types: constant localized pain, radicular pain, and axial pain⁴. Traditional pain management techniques involve a combination of pharmacotherapy, radiotherapy and surgical procedures⁴.

Axial pain, most frequently associated with mechanical instability of the spine or pathologic vertebral body fracture, is worsened by physical activity but relieved at rest⁵. Axial pain is generally treated by surgical stabilization of the spine⁵. Recent technological advances combined with innovative interventional radiology techniques can now offer alternative, less invasive treatment options for many patients with malignant vertebral body infiltration⁵.

In this review, the authors will discuss minimally invasive procedures used in palliative treatment of spinal and extraspinal metastases: vertebroplasty, kyphoplasty, osteoplasty, radiofrequency ablation, cryoablation, and transarterial embolization.

Methods

Percutaneous vertebroplasty

The procedure involves percutaneous access to the vertebral body with a large (11 or 13 gauge) introducer needle (cannula) and injection of the polymethyl methacrylate (PMMA) cement in a semiviscous

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Fig. 1. Interventional radiology suite with double C-arm angiography unit that enables biplane fluoroscopy. The percutaneous vertebroplasty procedure with cement injection is shown.

state into the vertebral body. The safest needle path at thoracic and lumbar level is transpedicular approach⁶. The anterolateral approach avoiding injury of the carotid-jugular complex is typically followed at cervical levels^{3,6}. The method was first described by Galibert *et al.*, who performed percutaneous acrylic cement injection for the treatment of aggressive vertebral body hemangioma⁷. The procedure that is usually carried out under local anesthesia combined with sedation is performed under fluoroscopic (x-ray) guidance. The

procedure must be carried out in an operating theater or interventional radiology suite under strict aseptic conditions. Biplane fluoroscopy (double C-arm angiography unit) in interventional radiology suite offers continuous two-dimensional guidance that enables optimal control and the safest access to the vertebral body (Fig. 1). This procedure can also be carried out using computed tomography (CT) in combination with fluoroscopy; however, most centers reserve this technique for selected cases⁴.

Thoracic and lumbar procedures are performed with the patient in prone position. The level to be treated is marked under fluoroscopy. A clear view of the targeting pedicle (with the entire cortical circumference) is mandatory before needle placement. The 'bull's eye' needle approach to the pedicle (perfect parallel alignment of the needle in tube direction, so the needle is seen as a spot) is simple and enables safe needle placement through the pedicle into the vertebral body. Transpedicular needle passage is a critical part of the procedure. Any error in the direction, e.g., crossing the medial pedicular wall, is potentially catastrophic, as entry into the spinal canal carries the risk of nerve root damage. Targeted needle position is achieved when the tip of the needle is in the ventral part of the vertebral body as close to the midline in coronal plane as possible (Fig. 2 a, b, c). Bone biopsy can be taken using coaxial technique through the same

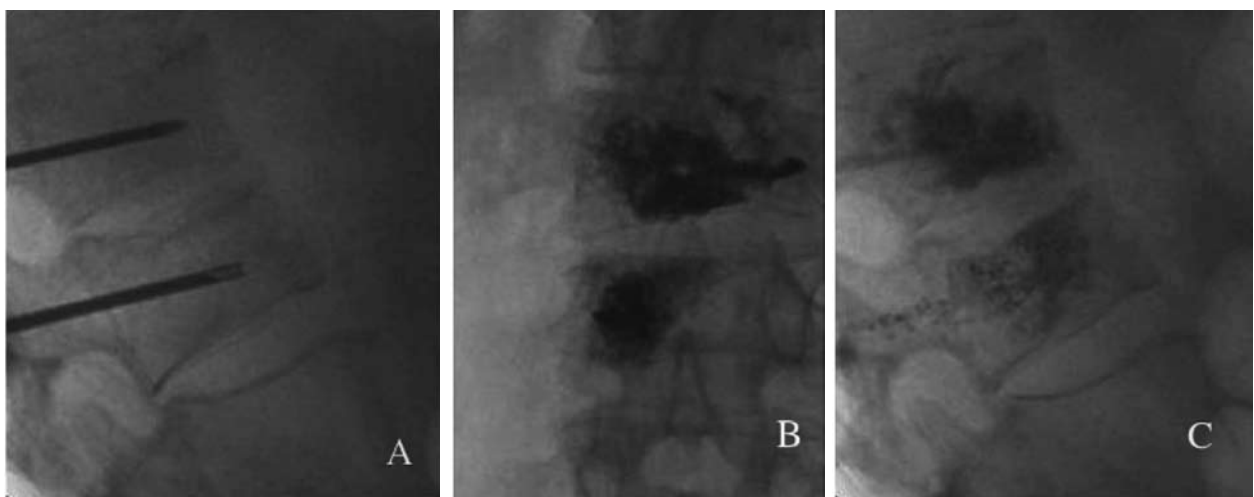


Fig. 2. Percutaneous vertebroplasty of Th12 and L1 vertebral bodies in a patient with pathologic compression fractures with unipedicular approach under fluoroscopy control. Lateral projection on fluoroscopy shows the position of the needles in the ventral part of the vertebral bodies (a); cement distribution in lateral and anteroposterior projection on fluoroscopy shows no leakage outside the vertebral bodies after the procedure (b, c).

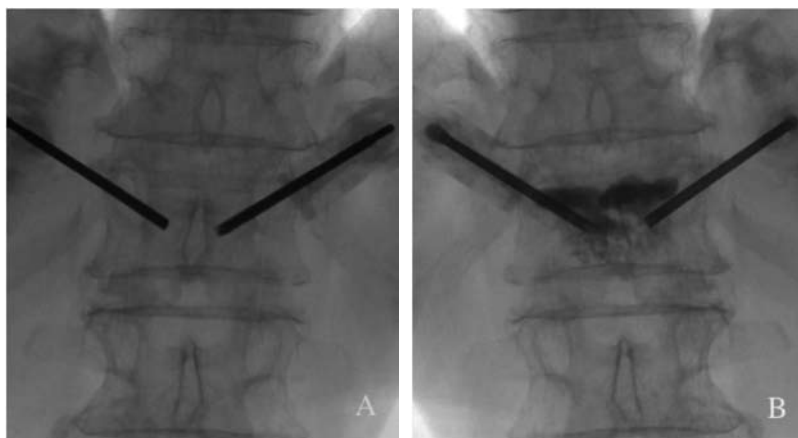


Fig. 3. Percutaneous vertebroplasty of T12 in a patient with metastatic renal cell carcinoma with bipedicular approach. The anteroposterior projection on fluoroscopy shows the position of the needles (a) that enabled distribution of the cement through the entire vertebral body (b). The patient presented with immediate and long-term symptom relief.

needle before the cement is injected. The two needle (bipedicular) approach is used when the position of the needle is in the lateral part of the vertebral body and the cement is not distributed through the entire vertebral body (Fig. 3 a, b). The cement is injected manually under continuous fluoroscopic control. The filling pressure must be as low as possible while still generating cement passage through the needle. Using this type of technique, the procedure can be stopped if any cement leakage in venous plexus or outside the vertebral body is noticed.

The overall risk associated with percutaneous vertebroplasty for malignant disease is $\leq 10\%$ ^{4,8,9}. The most frequent complication is local cement leakage. A risk factor for such a complication is a bone defect of the posterior vertebral wall or pedicle wall breach¹⁰. Although the majority of cement leakage are asymptomatic, severe neurological complication can result from leakage into the spinal canal¹¹. There is also the risk of pulmonary embolism caused by the cement that has entered the paravertebral venous plexus. The reported rate of pulmonary cement embolism is 3.4%¹². Pulmonary embolism may be symptomatic or asymptomatic^{13,14}. The occurrence of diffuse, extensive lung embolization is only possible when a considerable amount of cement is injected in a very low viscosity state¹⁴.

High viscosity cements have improved the uniformity of cement filling and decreased the rate of leakage¹⁵. Vertebroplasty has been shown to be extremely effective in improving pain from vertebral fractures. Within the first 48 hours after the procedure, an analgesic effect is achieved that persists for at least 6 months¹⁶. This effect is attributed to stabilization that results from preventing micromovements responsible

for vertebral pain. Additional effect of vertebroplasty is destruction of nerve endings by the exothermic reaction occurring during polymerization¹⁷. There is also a hypothesis that PMMA has an inherent tumoricidal or cytotoxic effect¹⁸.

The reported analgesic efficacy is 86% at 1 month, and 92% at 6 months¹². In the past three years, these results have been challenged and have become a subject of scientific and clinical debate¹⁹. This is mostly due to the results of two randomized, double blind, placebo-controlled trials published by Buchbinder *et al.*²⁰ and Kallmes *et al.*²¹. Nevertheless, these reports have been challenged by other reports^{22,23}, which are also concordant with our own results. However, there are significant differences in the risk taking, expectations, and perseverance in people who are willing to relegate their treatment to chance *versus* patients who refuse to participate²⁴. In general, there has also been an increase in the use of other, complementary methods to treat chronic musculoskeletal pain worldwide but, with some exceptions, there is no solid enough scientific evidence to support the use of these methods in musculoskeletal conditions²⁵.

Vertebroplasty is indicated in painful vertebral body tumors. In cancer patients, the procedure is used particularly in symptomatic treatment of osteolytic bone metastases and myeloma producing severe axial (non-radiating) pain due to fractured vertebrae. As vertebroplasty is intended only to treat pain and consolidate the weight-bearing bone, other specific tumor therapy should be given in conjunction when appropriate²⁶. The method could be combined with radiation therapy (performed before or after vertebroplasty). The method can be even simultaneously performed

with radiotherapy²⁷. Alternatively, CT image-guided procedure can be used as a platform technology for near-simultaneous spinal (and extraspinal) stereotactic radiotherapy²⁸.

Absolute contraindications for vertebroplasty are infection, uncorrectable coagulopathy, symptomatic spinal cord compression at the level of the fracture, severe cardiopulmonary disease, lack of surgical back up, or patient monitoring facilities. Relative contraindications are inability of the patient to lie prone for the duration of the procedure, acute burst fractures, and complete loss of vertebral height (vertebra plana)²⁹.

Kyphoplasty

Kyphoplasty was introduced in 2001. It is a modification of vertebroplasty employing a balloon tamp to restore vertebral height and create a cavity inside the vertebral body to accommodate the implanted cement³⁰. The balloon tamp is advanced and inflated through a 9-11 gauge cannula inserted as in vertebroplasty. The goal is to correct or prevent kyphotic deformities after loss of vertebral height. However, the fundamental principle of both vertebroplasty and kyphoplasty remains mechanical bone stabilization with cement injection³¹.

The advantages of kyphoplasty are restoration of vertebral body height and correction of kyphosis^{32,33}. The reported mean height restoration after kyphoplasty for compression fractures is around 3-5 mm at the center of the vertebral body³⁴.

In addition to providing rapid pain relief, balloon tamp kyphoplasty has the advantage of reducing acute fractures, allowing controlled cement placement under lower pressure, and improving deformity, which is especially beneficial in elderly patients for restoration of overall spinal sagittal alignment and kyphotic deformity³³. Additional advantage of kyphoplasty is less cement leakage compared to vertebroplasty^{33,35}.

Disadvantages of kyphoplasty as compared to vertebroplasty are that kyphoplasty is always performed under general anesthesia, longer duration of the pro-

cedure, and the cost of the procedure is 10 to 20 times higher^{32,33}.

According to data in the literature available, both vertebroplasty and kyphoplasty procedures showed no significant difference in pain relief after 6 months³⁶. The choice of the method for a particular clinical case, therefore, should be made with full knowledge of the advantages and shortcomings of both procedures.

Osteoplasty

Cementoplasty of the sacrum (sacroplasty) and acetabulum (acetabuloplasty) and other weight-bearing bones (osteoplasty in general) are procedural variants of percutaneous vertebroplasty aiming to palliate pain by cement reinforcement of malignant osteolytic lesions³². Effective pain management of painful insufficiency fractures or malignant osteolysis of the sacrum, the pubic rami, the ischial tuberosities and the acetabulum may be achieved with image guided injection of the cement³¹. The same principles apply for the extraspinal cementoplasty or osteoplasty as in percutaneous vertebroplasty. CT guidance is advocated for acetabuloplasty, whereas the 'bull's eye' fluoroscopic approach may be employed for pubic osteoplasty³² (Fig. 4). Injection of iodinated contrast before cementoplasty is advocated to predict distribution of cement and visualize the potential pathways of cement extravasation³². The potential complications include cement-induced injury of sensitive neurovascular structures like the obturator and pudendal nerve³⁷. Intra-articular cement leak into the hip joint has also

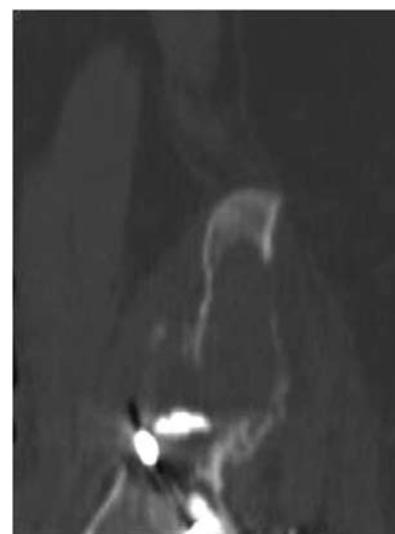


Fig. 4. Osteoplasty in a patient with painful osteolytic metastases of the iliac bone. The puncture of the iliac bone was performed under computed tomography (CT) control and cement was injected under continuous fluoroscopy control in the same interventional suite unit. The image shows distribution of the cement on control CT.

been described without any clinical significance^{37,38}. Cementoplasty of osteolyses located in the diaphysis of long weight-bearing bones like femur should be avoided because of inadequate bone consolidation and pathologic fractures. However, femoral head lesions have been successfully treated³⁸. The reported rates of pain relief after osteoplasty for extraspinal bone metastases are comparable to those of vertebroplasty³⁹.

Percutaneous radiofrequency ablation

Radiofrequency ablation (RFA) uses thermal energy to destroy tumor cells. In the musculoskeletal system, the method was first used to treat painful osteoid osteomas, benign bone tumors⁴⁰. The procedure starts with an introducer needle insertion into the vertebral body under fluoroscopic (or CT) guidance in the same way as described for percutaneous vertebroplasty. This procedure is also performed under local anesthesia combined with sedation. With the tip of the needle in the target position, the electrode is passed through the needle into the tumor (Fig. 5 a, b, c). The electrode is attached to a radiofrequency generator.

The high-frequency alternating current from the electrode generates marked agitation of the ions in the tissue that surrounds the uninsulated tip of the probe. The frictional heat results in thermal coagulation necrosis of the surrounding tissue^{4,41,42}. Roughly, the size of ablation correlates with the intensity and duration of energy deposition⁴⁰. The diameter of local

coagulation necrosis is a function of the local mean temperature^{42,43}. For effective heating throughout the tumor, it is necessary to achieve 60-100 °C and maintain it throughout the target volume for at least 4-6 min⁴¹. The types of the electrodes are plain, expandable, and cooled electrodes. Plain electrodes are used for the treatment of small lesions (<5 mm), expandable electrodes create large, spherical shapes up to 7 cm, and cooled electrodes can achieve coagulation diameter up to 3 cm⁴².

There is a risk of destroying non-target healthy tissue that surrounds the tumor. Therefore, thermal effects of radiofrequency heating on the adjacent soft and neural tissue must be considered before RFA is applied to spinal tumors⁴⁴. A margin of safety is provided in cases in which preserved cancellous or cortical bone is between the lesion and the spinal canal⁴⁵. Electrodes with short active tip (length of 1 cm) provide additional safety with less damage to the surrounding tissue⁴⁶.

About 80% of patients reported a decreased use of analgesics after RFA⁴⁷. The method produces rapid, significant and enduring pain control in bone metastases, still evident at one-year follow up in most cases, and elicits marked improvement in the quality of life of treated patients⁴⁸. Theories for its mechanism of action include destruction of sensory nerve fibers, reduction of lesion size, and destruction of tumor cells producing nerve-stimulating factors⁴.

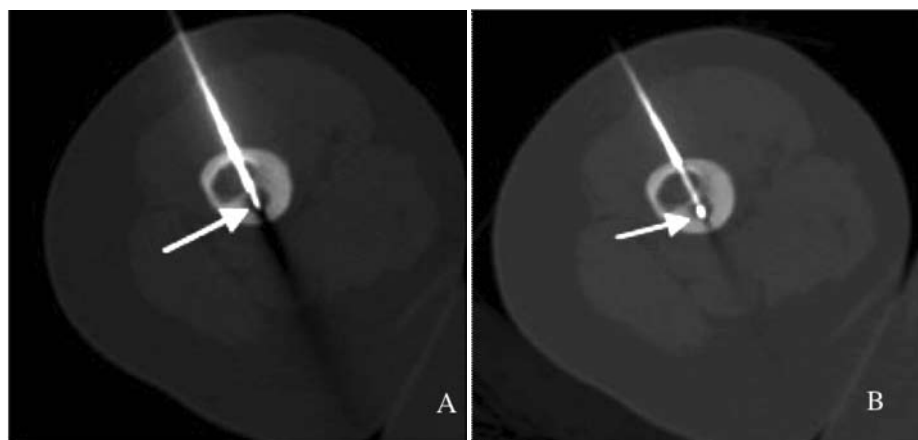


Fig. 5. Radiofrequency ablation of osteoid osteoma of the femur. The puncture pathway was determined under computed tomography control; the introducer needle was placed at the exact position of the tumor (white arrow) (a); radioablation probe was introduced through the introducer needle and placed into the nidus of the osteoid osteoma to perform ablation (white arrow) (b); available at: <http://www.health-writings.com>.

The percutaneous RFA is indicated as co-adjuvant palliative treatment in patients with bone metastases and who do not benefit from standard therapy⁴⁸. The method can be combined with percutaneous vertebroplasty that provides stabilization of the treated segment^{5,44}. There is also a positive effect of RFA on vertebroplasty. Data show that if RFA is carried out before vertebroplasty, the risk of cement extravasation is reduced⁴⁹. The aim of performing radiofrequency heat ablation before vertebroplasty is to destroy tumor tissue and to thrombose the paravertebral and intra-vertebral venous plexus, and thereby minimize the procedure-related complications⁴³.

Contraindications to percutaneous RFA are the same as described for percutaneous vertebroplasty. Relative contraindication exists in patients with extensive osteolysis with no intact cortex between the tumor and the spinal cord or nerve roots because of the potential for thermal injury to the adjacent neural tissue⁴⁵.

Cryoablation

Cryoablation has a long history of successful treatment of neoplasms in several organs and has also recently emerged as an exceptional method for the treatment of metastatic disease involving bone and soft tissue outside the liver and lung⁵⁰. The rationale for using cryoablation for this clinical need is based on its ability to treat often complex metastatic disease effectively, while preserving adjacent normal critical tissue⁵¹. Careful monitoring of the cryoablation margin is possible, due to the visibility of the ice ball on CT and magnetic resonance imaging (MRI), which is a key advantage of cryoablation over the other methods^{51,52}.

Cryoablation devices include percutaneous cryoprobes that deliver room temperature argon gas through a sealed, segmentally insulated probe. Rapid expansion of the gas in the sealed distal cryoprobe results in rapid cooling, reaching -100 °C at the probe tip within a few seconds. Small diameter probes (1.2-2.4 mm) allow percutaneous use of these devices⁵¹. Multiple cryoprobes may be placed in geometric configuration that provides best coverage of the tumor with particular attention being paid to the treatment of the bone-tumor interface while avoiding adjacent critical structures. In general, the probes are placed 2 cm apart within the tumor and 1 cm from the outer

tumor margin. A single freeze-thaw-freeze cycle is performed for each lesion, with a goal treatment time of 10-15 min⁵⁰. To avoid uncertain cell death with temperatures between 0 and -20 °C, repeated freeze-thaw-freeze cycles are needed. Indeed, ice crystals are mainly extracellular during the first freezing phase; during thawing phase, water diffuses into the intracellular compartment due to osmotic gradients, and the second freezing phase achieves intracellular ice crystals, leading to membrane rupture and cell death⁵³. The longer the duration of the thawing phase, the greater is the cell damage it causes⁵³. Repetition of the treatment cycle is associated with more extensive and more certain tissue destruction⁵⁴. Monitoring may be performed as frequently as every 2 min with limited non-contrast CT, although the ablation zone may also be seen on MRI^{50,52}. The ablation zone is identified as a well-margined low attenuation region along the distal shaft of the cryoprobe⁵¹. The outer edge of the ice, as seen on the body window at level settings (W400, L40) corresponds to 0 °C, with cell death reliably occurring 3 mm deep near the edge. For curative cryoablation, the margins of the ice ball should extend 3 to 5 mm beyond the tumor margins⁵³. The probes may be actively used until they reach approximately 25 °C, at which point they can be removed⁵¹. Recent studies report on the interest in cryoablation for palliative treatment of bone metastases, with very promising results and few complications^{51,55}.

Cryoablation is indicated in painful bone and soft tissue metastasis. The pain should be described by patients as at least moderate or severe and localized in one or two locations; patients with diffuse skeletal metastases are better served with systemic therapies⁵¹. Lesions should be osteolytic, mixed osteolytic-osteoblastic, or primary soft tissue component. Osteoblastic metastases require bone drill⁵¹. The required margin of safety between target lesion and vital structures depends on the ability to visualize adjacent critical structures, the use of technique to displace normal tissue, the use of thermal protection and monitoring devices, and experience of the interventional radiologist⁵¹.

The major advantage of cryoplasty is the possibility of precise monitoring of the treatment zone, which allows complete treatment of the lesion and preservation of the adjacent structures. It also allows the use of multiple cryoprobes simultaneously, thus enabling

generation of large ice balls (>8 cm) and the ability to shape the ablation zone according to the tumor. Cryoablation allows the additional option of tissue displacement with catheter guided balloons, which is not possible with heat-based methods due to thermal limitation of these devices.

The major disadvantage of cryoablation is that it is more time consuming compared to RFA (average procedure lasts for about 2 hours) and it may be more costly than RFA (the cost varies greatly depending on the size of the tumor).

The results of cryoablation treatment that are known so far are promising. On the Cleeland brief pain inventory⁵⁶, the mean score for worst pain decreased significantly in 43% of patients in 4 weeks, which is considered clinically significant⁵⁷. At 4 weeks of cryoablation, patient reported pain relief ranged from 50% to 100%, which compared favorably to RFA⁵¹.

Percutaneous transarterial embolization

The procedure involves percutaneous selective transarterial deliverance of the embolization agent for direct devascularization of a hypervascular tumor.

Transarterial embolization of spinal tumors was described in 1974 by Benati, who published first results of transfemoral selective embolization in the treatment of cranial and vertebro-spinal vascular malformations and tumors⁵⁸.

Selective catheterization of tumor's feeding artery/arteries is performed through the femoral artery access. The procedure that can be carried out under local anesthesia combined with sedation is performed under fluoroscopic guidance in an interventional radiology suite. The iodine contrast agent administered intra-arterially is visualized by fluoroscopy of the angiographic unit (C-arm). Digital subtraction angiography (DSA) is a method that enables subtraction of arteries from background tissue. With the DSA technique, the supraseductive catheterization of arteries that feed the tumor is possible using special microcatheters (with outer diameter up to 0.4 millimeters). With the tip of the microcatheter in the target position, the embolization material can be delivered to the tumor (Fig. 6 a, b).

Various embolic materials are available for transarterial embolization. They can be in solid state like

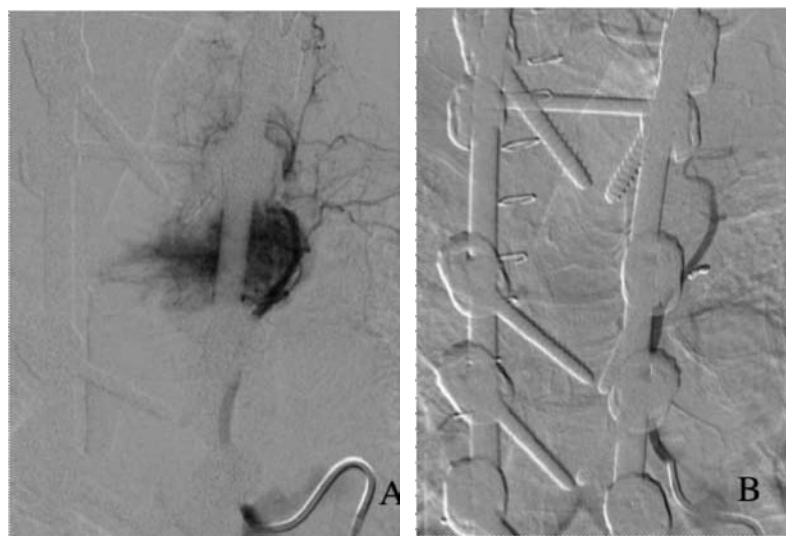


Fig. 6. Percutaneous transarterial embolization in a patient with multiple myeloma. The patient had already undergone surgical stabilization of the spinal column due to multiple pathologic fractures. However, because of the disease progression, another surgical stabilization was needed. The procedure was combined with preoperative percutaneous transarterial embolization. Supraseductive catheterization of the artery that supplied the highly vascular tumor of the Th2 vertebra as shown with digital subtraction angiography (a) enabled efficient preoperative embolization with polyvinyl alcohol particles and microcoils. Complete devascularization of the tumor is seen (b); there was significant reduction of blood loss during the surgery (with permission of D. Lovric).

particles (e.g., gelatin sponge, polyvinyl alcohol particles (PVA)) or coils, and in liquid state (alcohol, n-butyl cyanoacrylate (NCBA), ethylene-vinyl alcohol copolymer (Onyx)). Embolization with PVA particles is the most commonly used method. Gelatin sponge and coils or a combination are also used in the setting of potential collaterals necessitating flow diversion⁵⁹.

Spinal tumor embolization carries certain risks, including complications of vascular access (e.g., hematoma or pseudoaneurysm), radiation exposure, iodinated contrast, catheter manipulation (e.g., vessel dissection or rupture), or embolization (e.g., spinal or cerebral infarction)⁴⁵. Embolization of vertebral body tumors is potentially dangerous because of numerous vascular channels around the vertebral column. Non-target embolization can lead to catastrophic consequences. Intraprocedural angiographic visualization of collaterals and Adamkiewicz's artery is crucial. Occlusion of this artery can result in permanent neurologic deficit or even paraplegia.

The reported success rate of embolization is 37% (complete embolization of tumor) to 63% (partial embolization)⁶⁰.

The main indication for transarterial embolization in metastatic spinal disease is preoperative embolization. It represents a safe and effective procedure to decrease intraoperative blood loss^{59,60}. It can also be used as a palliative therapeutic option that may offer rapid relief of symptoms⁶¹.

There is only one absolute contraindication to embolization in spinal region. Visualization of any dangerous anastomoses is an absolute contraindication. Uncorrectable coagulopathy is the major relative contraindication. Other relative contraindications are renal insufficiency and allergy to iodinated contrast media.

Minimally invasive (percutaneous) treatment of metastatic spinal and extraspinal disease at University Medical Centre Ljubljana, Slovenia

Percutaneous vertebroplasty for malignant disease was started by the authors at the Clinical Institute of Radiology in the year 2011. As a method of choice, it has been used in all 21 cases of pathological and osteoporotic fractures (11 thoracic and 10 lumbar) during the last two years. The mean age of 13 patients (10 women and 3 men) was 68.2 (range 57-83) years.

However, the majority of oncology patients treated at our department (8/13, 61%) presented with insufficiency fractures, as a consequence of osteoporosis and also long-term medicamentous treatment (e.g., corticosteroid therapy). Metastatic renal cell carcinoma was the most frequent cause of pathologic (osteolytic) fractures in our patients. Pre-procedural MRI was used in all patients in order to confirm bone marrow edema as a sign of a fresh fracture. Percutaneous bone biopsy was used in three (23%) patients during vertebroplasty procedure. Among these patients, pathologic fractures were confirmed in two (66%) cases. Multiple level procedures were performed in five (38%) patients, two-level procedures in three patients, and three- and four-level procedures in one patient each. We achieved good cement distribution in vertebral body in all treated patients. No procedure related clinically important side effects were noticed (no leakage toward spinal canal or into intervertebral disks, and also no other inter-procedural complication or adverse reaction). Dramatic, immediate pain relief was achieved in the vast majority of cases. Immediate post-procedural significant pain relief was defined as reduction of pre-procedural visual analog scale (VAS) score, and was achieved in all our patients. Stabilization of fracture (preventing additional collapse) and analgesic effect was achieved in the majority of patients (11/13, 85%). However, fracture of adjacent vertebral body occurred in two (2/13, 15%) patients within two months of the procedure. While one of these patients was treated conservatively, additional vertebroplasty was performed in the other case. Therefore, our initial experience confirmed the effectiveness and safety of the procedure in oncologic patients.

Although the fact that percutaneous RFA has been performed at the Clinical Institute of Radiology, it is not yet routinely used for skeletal lesions. Our experiences with skeletal RFA are therefore limited. However, with the introduction of cryoablation, both thermoablation techniques will gain an important role in selected patients.

Percutaneous transarterial embolization has been routinely used in our institution for many years. Embolization of metastatic spinal and extraspinal disease has been most frequently used as preoperative procedure to reduce major blood loss during the operative procedure. Also, the method has been successfully

used in some benign skeletal tumors (e.g., aneurysmal bone cyst).

The major advantage of performing minimally invasive (percutaneous) treatment by interventional radiologists is a diagnostic imaging support by their own department. Namely, different imaging modalities (fluoroscopy, CT, MRI) can serve not only for pre- and post-procedural assessment, but also as an image guided tool.

Conclusion

Vertebroplasty and its modifications (kyphoplasty and extraspinal cementoplasty) as well as thermal ablation techniques (RFA and cryoablation) and transarterial embolization are successful minimally invasive methods for the treatment of metastatic spinal and extraspinal disease. The methods can be utilized as an additional or palliative treatment in selected patients. A combination of these methods as well as a combination with other surgical and nonsurgical treatments can be used.

References

- HAGE WD, ABOULAFIA AJ, ABOULAFIA DM. Incidence, location, and diagnostic evaluation of metastatic bone disease. *Orthop Clin North Am* 2000;31:515-28.
- WONG DA, FORNASIER L, MacNAB I. Spinal metastases: the obvious, the occult, and the imposters. *Spine* 1990;15:1-4.
- MONT'ALVERNE F, VALLÉE JN, CORMIERE, GUILLEVIN R, BARRAGAN H, JEAN B, *et al.* Percutaneous vertebroplasty for metastatic involvement of the axis. *Am J Neuroradiol* 2005;26(7):1641-5.
- KASSAMALI RH, GANESHAN A, HOEY ET, CROWE PM, DOUIS H, HENDERSON J. Pain management in spinal metastases: the role of percutaneous vertebral augmentation. *Ann Oncol* 2011;22(4):782-6.
- GEORGY BA. Metastatic spinal lesions: state-of-the-art treatment options and future trends. *Am J Neuroradiol* 2008;29(9):1605-11.
- HERAN MK, LEGIEHN GM, MUNK PL. Current concepts and techniques in percutaneous vertebroplasty. *Orthop Clin North Am* 2006;37(3):409-34.
- GALIBERT P, DERAMOND H, ROSAT P, Le GARS D. Preliminary note on the treatment of vertebral angioma by percutaneous acrylic vertebroplasty. *Neurochirurgie* 1987;33(2):166-8.
- GANGI A, SABHARWAL T, IRANI FG, BUY X, MORALES JP, ADAM A. Quality assurance guidelines for percutaneous vertebroplasty. *Cardiovasc Interv Radiol* 2006;29(2):173-8.
- DERAMOND H, DEPRIESTER C, GALIBERT P, Le GARS D. Percutaneous vertebroplasty with polymethylmethacrylate. Technique, indications, and results. *Radiol Clin North Am* 1998;36(3):533-46.
- BARBANTI BRÒDANO G, CAPPUCCIO M, GABBARRINI A, BANDIERA S, De SALVO F, COSCO F, *et al.* Vertebroplasty in the treatment of vertebral metastases: clinical cases and review of the literature. *Eur Rev Med Pharmacol Sci* 2007;11:91-100.
- LEE BJ, LEE SR, YOO TY. Paraplegia as a complication of percutaneous vertebroplasty with polymethylmethacrylate: a case report. *Spine* 2002;27:419-22.
- CALMELS V, VALLEE JN, ROSE M, CHIRAS J. Osteoblastic and mixed spinal metastases: evaluation of the analgesic efficacy of percutaneous vertebroplasty. *Am J Neuroradiol* 2007;28:570-4.
- JANG JS, LEE SH, JUNG SK. Pulmonary embolism of polymethylmethacrylate after percutaneous vertebroplasty: a report of three cases. *Spine* 2002;27:416-8.
- BERNHARD J, HEINI PF, VILLIGER PM. Asymptomatic diffuse pulmonary embolism caused by acrylic cement: an unusual complication of percutaneous vertebroplasty. *Ann Rheum Dis* 2003;62:85-6.
- BAROUD G, CROOKSHANK M, BOHNER M. High-viscosity cement significantly enhances uniformity of cement filling in vertebroplasty: an experimental model and study on cement leakage. *Spine* 2006;31(22):2562-8.
- CORTET B, COTTEN A, BOUTRY N, DEWATRE F, FLIPO RM, DUQUESNOY B, *et al.* Percutaneous vertebroplasty in patients with osteolytic metastases or multiple myeloma. *Rev Rhum Engl Ed* 1997;64:177-83.
- BARRAGÁN-CAMPOS HM, VALLÉE JN, LO D, CORMIER E, JEAN B, ROSE M. Percutaneous vertebroplasty for spinal metastases: complications. *Radiology* 2006;238(1):354-62.
- San MILLAN RUIZ D, BURKHARDT K, JEAN B, MUSTER M, MARTIN JB, BOUVIER J, *et al.* Pathology findings with acrylic implants. *Bone* 1999;25(2):85-90.
- MILLER FG, KALLMES DF, BUCHBINDER R. Vertebroplasty and the placebo response. *Radiology* 2011;259(3):621-5.
- BUCHBINDER R, OSBORNE RH, EBELING PR, *et al.* A randomized trial of vertebroplasty for painful osteoporotic vertebral fractures. *N Engl J Med* 2009;361(6):557-68.
- KALLMES DF, COMSTOCK BA, HEAGERTY PJ, *et al.* A randomized trial of vertebroplasty for osteoporotic spinal fractures. *N Engl J Med* 2009;361(6):569-79.
- FISHER CG, VACCARO AR, THOMAS KC, ANGEVINE PD, MULPURI K, PATEL AA, PRASAD SK, WHANG PG. Evidence based recommendations for spine surgery. *Spine* 2010;(35):678-86.

23. HIRSCH JA, HIRSCH AE, ZOARSKI GH, BROOK AL, STONE JA, HECK DV, YOO AJ. Social responsibility in medical reporting. *J NeuroInterv Surg* 2010;(2):217-8.
24. CHEN LH, LAI PL, CHEN WJ. Current status of vertebroplasty for osteoporotic compression fracture. *Chang Gung Med J* 2011;34(4):352-9.
25. GRAZIO S, BALEN D. Complementary and alternative treatment of musculoskeletal pain. *Acta Clin Croat* 2001;50:513-30.
26. GANGI A, GUTH S, IMBERT JP, MARIN H, DIETEMANN JL. Percutaneous vertebroplasty: indications, technique, and results. *RadioGraphics* 2003;23(2):e10.
27. WENZ F, SCHNEIDER F, NEUMAIER C, KRAUSTIEFENBACHER U, REIS T, SCHMIDT R, *et al.* Kypho-IORT – a novel approach of intraoperative radiotherapy during kyphoplasty for vertebral metastases. *Radiat Oncol* 2010;5:11.
28. SHIU AS, CHANG EL, YE JS, LII M, RHINES LD, MENDEL E, *et al.* Near simultaneous computed tomography image-guided stereotactic spinal radiotherapy: an emerging paradigm for achieving true stereotaxy. *Int J Radiat Oncol Biol Phys* 2003;57(3):605-13.
29. HALPIN RJ, BENDOK BR, LIU JC. Minimally invasive treatments for spinal metastases: vertebroplasty, kyphoplasty, and radiofrequency ablation. *J Support Oncol* 2004;2:339-351.
30. LIEBERMAN IH, DUDENEY S, REINHARDT MK, BELL G. Initial outcome and efficacy of “kyphoplasty” in the treatment of painful osteoporotic vertebral fractures. *Spine* 2001;26(14):1631-8.
31. PHILLIPS FM, HO E, CAMPBELL-HUPP M, McNALLY T, TODD WETZEL F, GUPTA P. Early radiographic and clinical results of balloon kyphoplasty for the treatment of osteoporotic vertebral compression fractures. *Spine* 2003;28(19):2260-5.
32. KATSANOS K, SABHARWAL T, ADAM A. Percutaneous cementoplasty. *Spinal interventions*. ESIR, July 9-10, 2010, Strasbourg (FR).
33. DENARO V, LONGO UG, MAFFULLI N, DENARO L. Vertebroplasty and kyphoplasty. *Clin Cases Bone Metab* 2009;6(2):125-30.
34. MATHIS JM, ORTIZ AO, ZOARSKI GH. Vertebroplasty *versus* kyphoplasty: a comparison and contrast. *Am J Neuroradiol* 2004;25(5):840-5.
35. 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(3):488-97.
36. LIU JT, LIAO WJ, TAN WC, LEE JK, LIU CH, CHEN YH, *et al.* Balloon kyphoplasty *versus* vertebroplasty for treatment of osteoporotic vertebral compression fracture: a prospective, comparative, and randomized clinical study. *Osteoporos Int* 2010;21(2):359-64.
37. KELEKIS A, LOVBLAD KO, MEHDIZADE A, SOMON T, YILMAZ H, WETZEL SG, *et al.* Pelvic osteoplasty in osteolytic metastases: technical approach under fluoroscopic guidance and early clinical results. *J Vasc Interv Radiol* 2005;16(1):81-8.
38. HIERHOLZER J, ANSELMETTI G, FUCHS H, DEPRIESTER C, KOCH K, PAPPERT D. Pelvic osteoplasty as a treatment for painful malignant bone lesions of the pelvis and femur. *J Vasc Interv Radiol* 2003;14(6):773-7.
39. WHITLOW CT, MUSSAT-WHITLOW BJ, MATTERN CW, BAKER MD, MORRIS PP. Sacroplasty *versus* vertebroplasty: comparable clinical outcomes for the treatment of fracture-related pain. *Am J Neuroradiol* 2007;28(7):1266-70.
40. BAREI DP, MOREAU G, SCARBOROUGH MT, NEEL MD. Percutaneous radiofrequency ablation of osteoid osteoma. *Clin Orthop* 2000;373:115-24.
41. OFLUOGLU O. Minimally invasive management of spinal metastases. *Orthop Clin North Am* 2009;40(1):155-68.
42. WIDMANN G, BODNER G, BALE R. Tumour ablation: technical aspects. *Cancer Imaging* 2009;9:63-7.
43. BUY X, BASILE A, BIERRY G, CUPELLI J, GANGI A. Saline-induced bipolar radiofrequency ablation of high-risk spinal and paraspinous neoplasms. *AJR Am J Roentgenol* 2006;186(Suppl 5):323-6.
44. SCHAEFER O, LOHRMANN C, MARKMILLER M, UHRMEISTER P, LANGER M. Technical innovation. Combined treatment of a spinal metastasis with radiofrequency heat ablation and vertebroplasty. *AJR Am J Roentgenol* 2003;180(4):1075-7.
45. DUPUY DE, HONG R, OLIVER B, GOLDBERG SN. Radiofrequency ablation of spinal tumors: temperature distribution in the spinal canal. *AJR Am J Roentgenol* 2000;175:1263-6.
46. ADACHI A, KAMINOU T, OGAWA T, KAWAI T, TAKAKI Y, SUGIURA K, *et al.* Heat distribution in the spinal canal during radiofrequency ablation for vertebral lesions: study in swine. *Radiology* 2008;247(2):374-80.
47. BELFIORE G, TEDESCHI E, RONZA FM, BELFIORE MP, Della VOLPE T, ZEPPELELLA G, *et al.* Radiofrequency ablation of bone metastases induces long-lasting palliation in patients with untreatable cancer. *Singapore Med J* 2008;49(7):565-70.
48. CALLSTROM MR, CHARBONEAU JW, GOETZ MP, RUBIN J, WONG GY, SLOAN JA. Painful metastases involving bone: feasibility of percutaneous CT- and US-guided radiofrequency ablation. *Radiology* 2002;224:87-97.
49. CHI JH, GOKASLAN ZL. Vertebroplasty and kyphoplasty for spinal metastases. *Curr Opin Support Palliat Care* 2008;2(1):9-13.
50. CALLSTROM MR, ATWEL TD, CHARBONEAU JW, FARRELL MA, GOETZ MP, RUBIN J, *et al.* Painful metastases involving bone: percutaneous image-guided cryoablation-prospective trial interim analysis. *Radiology* 2006;241:572-80.

51. CALLSTROM MR, KURUP AN. Percutaneous ablation for bone and soft tissue metastases – why cryoablation? *Skeletal Radiol* 2009;38:835-9.
52. BELAND MD, DUPUY DE, MAYO-SMITH WW. Percutaneous ablation of renal tumors: cryoablation *versus* radiofrequency ablation – initial observations. *Radiology* 2005;184:926-30.
53. GANGI A, BUY X. Percutaneous bone tumor management. *Semin Interv Radiol* 2010;27(2):124-36.
54. GAGE AA, BAUST JG. Cryosurgery for tumors. *J Am Coll Surg* 2007;205:342-56.
55. ULLRIK SR, HERBERT JJ, DAVIS KW. Cryoablation in the musculoskeletal system. *Curr Probl Diagn Radiol* 2008;37:39-48.
56. CLEELAND CS, GONIN R, HATFIELD AK, *et al.* Pain and its treatment in outpatients with metastatic cancer. *N Engl J Med* 1994;330:592-6.
57. FERRAR JT, YOUNG JP Jr, LaMOREAUX L, WERTH JL, POOLE RM. Clinical importance of changes in chronic pain intensity measures on an 11-point numerical pain rating scale. *Pain* 2001;94:149-58.
58. BENATI A, Dalle ORE G, Da PIAN R, BRICOLO A, MASCHIO A, PERINI S. Transfemoral selective embolisation in the treatment of some cranial and vertebro-spinal vascular malformations and tumours: preliminary results. *J Neurosurg Sci* 1974;18:233-8.
59. WILSON MA, COOKE DL, GHODKE B, MIRZA SK. Retrospective analysis of preoperative embolization of spinal tumors. *AJNR Am J Neuroradiol* 2010;31(4):656-60.
60. SCHMIDT R, RUPP-HEIM G, DAMMANN F, UL-RICH C, NOTHWANG J. Surgical therapy of vertebral metastases. Are there predictive parameters for intraoperative excessive blood loss despite preoperative embolization? *Tumori* 2011;97(1):66-73.
61. SMIT JW, VIELVOYE GJ, GOSLINGS BM. Embolization for vertebral metastases of follicular thyroid carcinoma. *J Clin Endocrinol Metab* 2000;85(3):989-99.

Sažetak

MINIMALNO INVAZIVNO (PERKUTANO) LIJEČENJE METASTATSKE SPINALNE I EKSTRASPINALNE BOLESTI – PREGLEDNI ČLANAK

V. Salapura i M. Jeromel

Metastatski tumori su najčešća zloćudna bolest kostiju. Mnogi bolesnici s metastazama kralježnice dolaze s bolovima i patološkim prijelomima. Razvoj intervencijske radiologije omogućio je alternativno i manje invazivno liječenje ovih bolesnika. U članku se prikazuju minimalno invazivni (perkutani) zahvati koji se danas primjenjuju: vertebroplastika, kifoplastika, osteoplastika, radiofrekvencijska ablacija, krioblacija i transarterijska embolizacija. Potom se raspravlja o indikacijama, kontraindikacijama, rezultatima i komplikacijama ovih postupaka. Prema našim saznanjima iz literaturnih podataka, minimalno invazivne tehnike su uspješne u liječenju metastatske spinalne i ekstraspinale bolesti te se mogu rabiti kao alternativa standardnim kirurškim i ne-kirurškim zahvatima.

Ključne riječi: *Koštani tumori, metastaze; Kralježnica, tumori – metastaze; Vertebroplastika – metode; Kifoplastika; Ablacijske tehnike; Kriokirurgija; Transarterijska kemoembolizacija; Palijativna skrb*