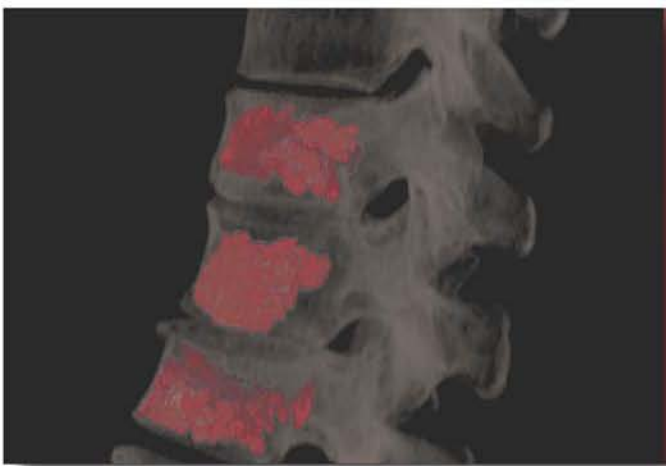
Chapter



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General Introduction & Outline of the Thesis

General Introduction

The History of Percutaneous Vertebroplasty

Percutaneous VertebroPlasty (PVP) involves the percutaneous injection of liquid bone cement, usually PolyMethylMethAcrylate (PMMA) and an opacifier (barium or zirconium oxide) into the inter-trabecular marrow space of a vertebral body.

Vertebroplasty was initially developed to be used in combination with an open surgical procedure to fill large voids as a result of tumour resection. In 1984, Galibert and Deramond performed the first ever documented PVP at the University Hospital of Amiens, France.[1] The procedure was used in a patient with severe cervical pain, due to a large vertebral haemangioma encompassing the entire C2 vertebral body. A 15-gauge needle was inserted and acrylic cement was injected into the C2 vertebral body via an anterolateral approach. This case, as published in 1987, reports complete pain relief in this patient.[1]

A paper in the *American Journal of Neuroradiology* in November 1997,[2] describing a trial from the University of Virginia, which comprised 29 patients followed over a period of three-years, with promising outcomes of PVP in treatment of Osteoporotic Vertebral Compression Fractures (OVCFs), prompted a sudden and major increase in the number of PVP procedures being performed.

Next to the "traditional" PVP, a comparable procedure encompassing PVP in combination with an inflatable balloon tamp (often referred to as kyphoplasty (KP)), arose in the early 1990s and shows comparable clinical outcomes.[3] The evidence for performing kyphoplasty is however beyond the scope of this thesis and therefore will not be discussed.

Percutaneous Vertebroplasty: Performing the Procedure

PVP can be performed in multiple ways. In some institutions, the procedure is performed under general anaesthesia using a single C-arm in the operating room. In our institution however, the procedure is performed under conscious sedation using bi-plane fluoroscopy in a radiological intervention suite. Bellow the procedure, as performed in our institution (Leiden University Medical Center), is briefly described.

The patient is admitted at the day-care department and 30 minutes after oral pain medication (Symoron 5mg and Paracetamol 1000mg), transferred to the radiology department. The patient is placed in prone position on a standardized cushion, in such a way that the regions caudally and cranially from the fractured vertebra(e) are supported. The patient is prepared and draped in a sterile fashion. Conscious sedation is administered using injectable Fentanyl and Midazolam (doses depending on weight and procedure duration). During the procedure, saturation, blood pressure and heart rate are continuously monitored. Using Bi-plane fluoroscopy **(Figure 1)**, the fractured level is identified.

Figure 1. Bi-plane fluoroscopy set-up. Important advantage of this system is the possibility of direct manipulation of the position of the x-ray tubes by the specialist performing the intervention using the sterile dressed control panel.

High quality fluoroscopy is mandatory in order to safely perform PVP. First the lateral X-ray tube is positioned in such a way that the caudal pedicle arches are superimposed and the upper and lower endplate will project as parallel as possible on the fluoroscopy image (depending on the grade of vertebral collapse) **(Figure 2)**.

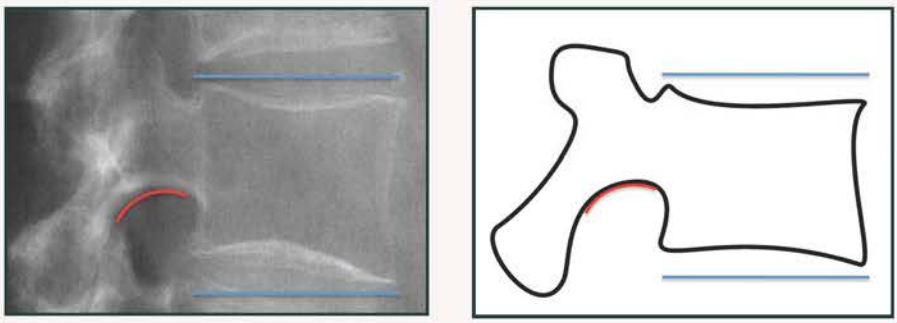

Figure 2. Superimposition of the pedicles (red lines) and parallel projection of the endplates (blue lines).

Next, in antero-posterior (AP) direction, the spinal processus are projected in the centre of the vertebral body and the pedicles should project over the upper third of the vertebral body. The projection of the "pedicle ring" results from projection of the isthmus of the pedicle **(Figure 3)**.

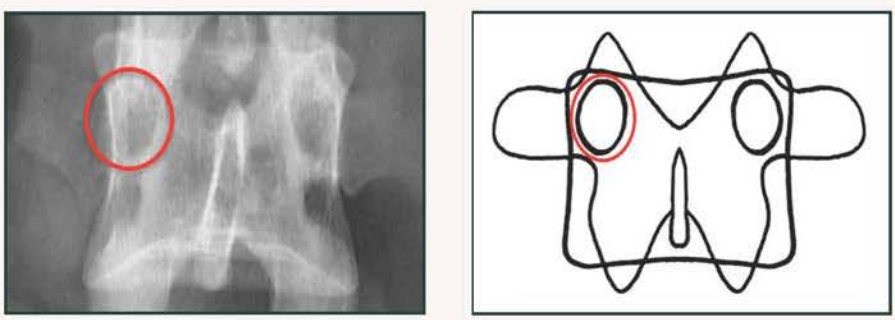

Figure 3. AP projection of the vertebral body (left), red circle: projection of the isthmus of the pedicle at the fluoroscopy image. Projection of the vertebral body (right), red circle: projection of the isthmus of the pedicle.

Local anaesthesia is achieved by injection of Lidocaine 1%. The position of the thin needle used for lidocaine injection determines the direction of the needle tract during fluoroscopy. This tract will be used for introduction of the large beveled PVP needle. Thus optimal introduction through the soft-tissues, without repeated placement of the large diameter (10G) PVP needle can be obtained. The preferred entrance is at ten-o-clock for the left pedicle, and two-o-clock for the right pedicle at the cranio-lateral border of the pedicle.

Under biplane fluoroscopy guidance and using a small mallet, one (preferred) or two needles are gently introduced into the vertebral body through a trans- or extra-pedicular route (depending on the level to be treated).

The trans-pedicular route is the easiest and safest route to the vertebral body in the lumbar spine. During the insertion of the needle into the vertebral body, the cortex of the pedicle surrounds the needle. However due to the position and angulation of the pedicles of the thoracic vertebral body and due to the fact that these (higher) thoracic vertebral bodies have a more pronounced apex, a trans-pedicular route is not advised for the (higher) thoracic vertebras. To access the (higher) thoracic spine, usually the extra-pedicular approach is used. For extra-pedicular approach the needle is inserted between the lateral margin of the pedicle of the thoracic vertebrae and the rib head.

During insertion of the needle, the beveled tip can be used to gain easy access to the pedicle by pointing the bevel laterally. When the needle has penetrated into the pedicle, prevention of perforation of the medial pedicle wall can be obtained by rotating the beveled side of the needle 180° to the medial pedicle wall **(Figure 4).**

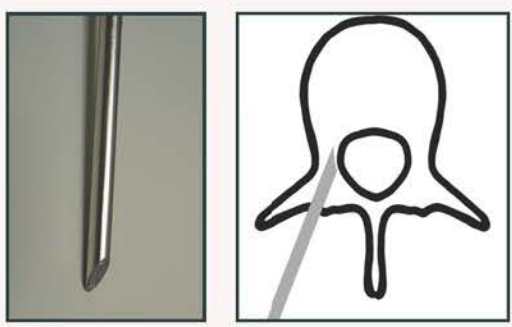

Figure 4. The beveled needle tip design facilitates easy and safe access to the vertebral body without penetration of the medial pedicle wall.

When lateral fluoroscopy shows that the tip of the needle has passed beyond 50% of the length of the pedicle, and PA projection shows a position of the needle lateral to the medial pedicle wall, a safe entrance into the vertebral body has been achieved.

At our institution, vertebral body bone biopsy and vertebroplasty are performed in one session using the following technique: the biopsy needle is inserted through the vertebroplasty needle just after penetration of the vertebral

body. The biopsy needle is withdrawn and the vertebroplasty needle is advanced through the same needle tract (see also, **Chapter 3** of *this thesis*). The preferred position of the needle is just lateral to the middle of the anterior one third of the vertebral body. If this position cannot be achieved, a second needle can be inserted through the contra-lateral pedicle. However placement of a second needle can also be done at a later stage during the procedure in case of inadequate cement interdigitation through the first needle.

The PMMA cement is prepared and transferred to an injector. The air is eliminated from the system. After 2-4 minutes after the start of cement mixing (depending on the viscosity of the cement and on the room temperature), the cement has reached its proper viscosity (toothpaste-like), and is ready to be injected. The cement is than injected slowly and carefully under constant bi-plane fluoroscopic imaging in order to achieve good filling of the intertrabecular space of the vertebral body and thus a minimal chance of major cement.

The injector is disconnected from the needle. Twelve to fourteen minutes after mixing, the needle is twisted to separate the tip from the cement. Then the needle(s) is (are) removed from the vertebral body. A post-procedural CT-scan is performed and the patient is placed in bed for transport to the ward. The post-procedural hospital stay is a minimum of 3 hours. Fast reactivation of the patient is started after the effect of the fentanyl and midazolam has ended, additional bed rest is not mandatory. When the overall clinical condition permits, the patient is discharged.

The Indications for Percutaneous Vertebroplasty

Although vertebroplasty was first used in spinal tumour surgery, the spectrum of indications for performing PVP has been increased since then. The procedure is also used for painful pathological compression fractures of other aetiologies, like trauma, aggressive vertebral haemangioma **(Figure 5)**, multiple myeloma **(Figure 6)** or bone metastasis.[4-8] PVP can offer mechanical stability to vertebral bodies, which are weakened by tumour invasion, and prevent further bone destruction when bone cement is injected between the trabeculae of the remaining unaffected bone.

Patients with disseminated disease and spinal metastasis and patients with primary vertebral malignant disease, who are non eligible candidates for extensive open surgery due to a combination of co-morbidity caused by malignant disease itself or due to (chemo)therapy, but are suitable candidates for a minimal

invasive procedure like PVP. Furthermore, the fact that PVP is performed in day-care and has a low morbidity rate and a quick potential pain relief, makes it an acceptable investment of time for patients with a short life expectancy.

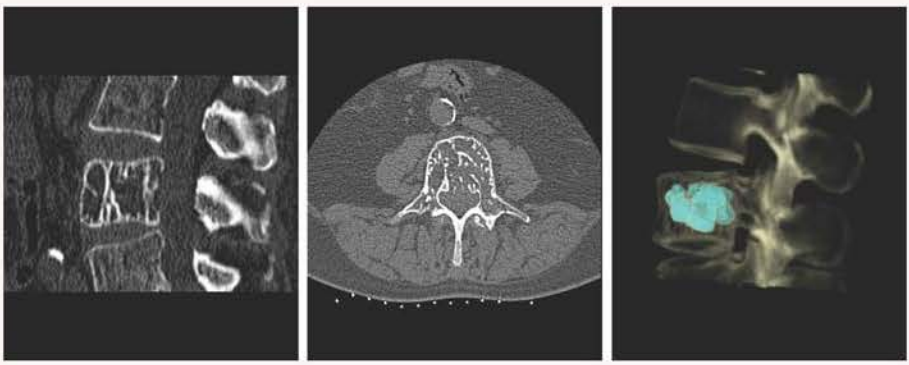

Figure 5. Painful pending vertebral collapse due to an aggressive haemangioma treated with PVP. From left to right: sagittal and axial CT-reconstruction both showing the specific trabecular destruction leading to a typical cement filling pattern as seen at a 3D CT-reconstruction (far right).

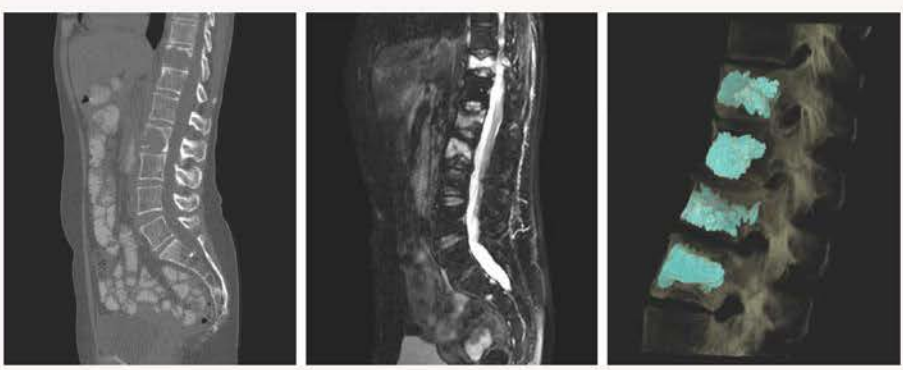

Figure 6. Vertebral destruction due to multiple myeloma, treated with PVP. From left to right: Sagittal CT-reconstruction showing extensive destruction of Th11 and L2. Sagittal reconstruction T2 MRI showing BME, most pronounced at Th11 and L2. Post-procedural 3D CT-reconstruction.

Due to its high incidence, compared to the above-mentioned indications, a painful compression fracture due to osteoporosis is the most common indication for PVP. The indication triad for PVP in OVCFs at our institution consists of I) incapacitating pain at the fractured level, with focal point tenderness, which increases when pressure is applied to the spinous process of the fractured vertebra,[10,11] II) unresponsiveness to at least 6-8 weeks of conservative treatment[9] and III) Bone Marrow Edema (BME) in the fractured vertebral body diagnosed at MR Imaging (see also, **Chapter 2** of *this thesis*).[12-14] **(Figure 7)**

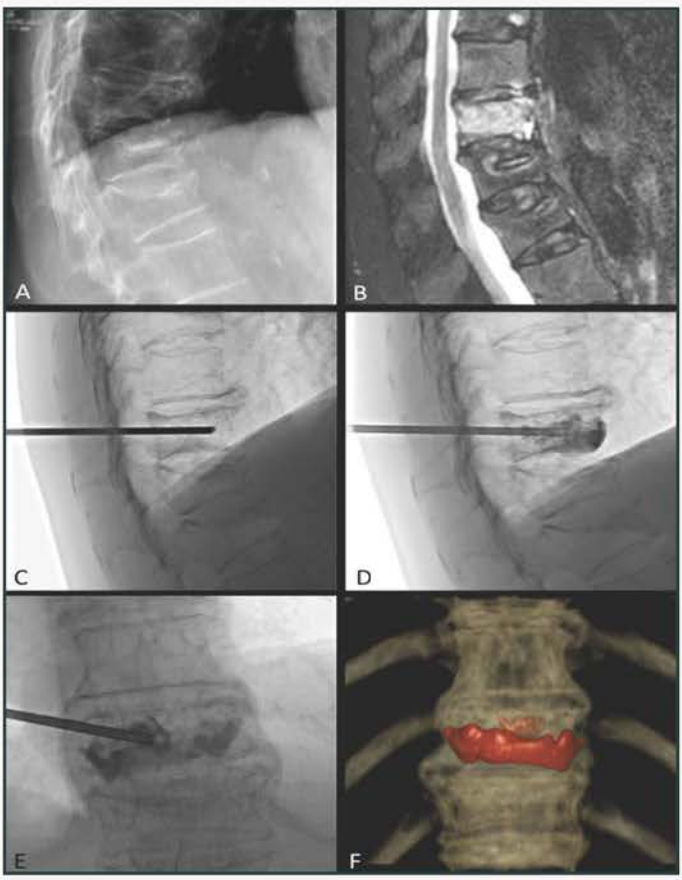

Figure 7. Example of a patient with multiple OVCFs as seen on the plain radiograph (A). On MR Imaging only one vertebra shows intravertebral BME (B). Lateral fluoroscopy images (C) and (D) show insertion of the needle and injection of the bone cement respectively. AP fluoroscopy image of cement injection (E) and 3D CT-reconstruction of the treated vertebra with cement (depicted in red).

Osteoporotic Vertebral Compression Fractures

The Osteoporotic Vertebral Compression Fracture (OVCF) is, with an estimated prevalence in the Netherlands of 18% for men and 22% for women above the age of 55 years, the most common complication of osteoporosis.[15-18]

In the year 2000, Dutch hospitals registered over 40.000 new vertebral fractures due to primary or secondary osteoporosis and with the ageing population it is expected that this number will increase throughout the upcoming years.[19] The Dutch population is expected to have the highest absolute increase of the number of OVCFs in the twenty-first century, compared to the other members of the European Union,[19]

Two thirds of the OVCFs have no clinical symptoms, they are "silent" fractures and are asymptomatic and as such there is no need for direct medical attention other than screening and treatment for osteoporosis in order to reduce the chance of new fractures.[20, 21]

In the group of patient with clinical symptoms due to an OVCF (one-third of all patients with a OVCF), pain is the most striking feature of the fracture. Next to pain, diminished mobilization is caused by progressive kyphosis, which in turn gives a decrease in lung capacity, with a subsequent decreased physical condition, which eventually results in an increase of bone loss, which is again the first step in a vicious circle leading to more OVCFs.[22, 23]

Treatment of Painful Osteoporotic Vertebral Compression Fractures

In 80-85% of the acute symptomatic patients, pain will disappear with conservative treatment within 6-8 weeks after initiation of treatment.[24-26] In the Netherlands, conservative treatment is therefore the preferred initial treatment in patients with an acute symptomatic OVCF without neurological symptoms. Conservative therapy involves a short period of bed rest (for a few days) and administration of oral analgesics and, optionally, short-term use of a thoraco-lumbar brace in order to achieve reduction of pain.[27] In case of neurological symptoms due to spinal stenosis, an open decompression combined with posterior stabilisation using pedicle screws, and vertebroplasty of the anterior vertebral column can be the treatment of choice.

Patients without neurological deficit, and no reduction of pain after 8 weeks of conservative treatment have a high chance of ending in a chronic circle of repeated pain attacks, with intermittent temporary pain relieve of a period for

up to two years.[24] For this group constituting 15-20% of the symptomatic OVCFs, i.e. patients with fractures refractive to conservative treatment, PVP can, after a careful workup, be the treatment of choice.

Outcome in Osteoporotic Vertebral Compression Fractures

Because of its reported fast analgesic effects, high effectiveness, low complication rate and relatively low cost, PVP has emerged as a widely used minimal invasive treatment of painful OVCFs over the past two decades.[28] The effect of PVP for OVCFs on pain is reported to be fast and reaches a plateau phase within a few days after the procedure.[29] After this period, the pain-scores do not change (see also, **Chapter 4** of *this thesis*).[30-33]

A meta-analysis of 60 studies reporting pre- and post-operative Visual Analogue Scale (VAS) scores (in which 10 represents excruciating pain) showed a mean pre-operative VAS of 8.36 (SD±0.78) and a mean post-operative VAS of 2.86 (SD±1.09). A mean and significant change in pain of 5.68 (SD±1.24)) on the VAS scale was found after PVP.[3]

Unfortunately, severe methodological problems exist in published studies so far. Most studies focus only on (often short term) pain outcome and do not report the use of any type of validated questionnaires reporting general Quality of Life, making it impossible to compare the PVP procedure with other (non- or minimal-invasive) procedures (see also, **Chapter 4** of *this thesis*). Furthermore, the majority of papers describe populations that are a case mix of "acute" (fracture age < 8 weeks) and "long-standing" (fracture age >8 weeks) OVCFs. The former having frequently a favourable natural course (there is a high chance that an acute OVCF will heal even without treatment).

Complications in Osteoporotic Vertebral Compression Fractures

The rate of clinically relevant complications after PVP for OVCFs is low. Complication rates reported range between 1.6% and 2.8%.[34] Most of these clinically relevant complications are due to leakage of bone cement (see also, **Chapter 5 & 6** of *this thesis*). Severe complications are rare and occur mainly in cases of high-volume cement leakage and are mainly reported in case reports.[35-38] Leakage of cement into the neural foramen or spinal canal can cause neurological injury.[39] Procedure related complications unrelated to cement leakage include; misplacement of the needle, rib fractures, pneumothorax, fracture of spinous process or pedicle, subcutaneous paravertebral haematoma and infection.[32, 40-45]

Aim and Outline of this Thesis

This thesis focuses on indications for and the clinical outcome of PVP for the treatment of long-standing OVCFs (i.e. after more than 8 weeks after onset of symptoms). Secondly, emphasis is made on the value of vertebral body biopsy during the vertebroplasty procedure in order to aid in early diagnosis of unexpected conditions. Thirdly, in line with the worldwide emerging registration and control of medical implants, emphasis is put on the need for careful registration of cement leakages, since these count for the largest number of clinically relevant complications of the vertebroplasty procedure.

Chapter Outline of this Thesis

The correlation between the amount of BME and the clinical outcome (pain) of PVP is discussed in **Chapter 2.** In **Chapter 3**, the outcome of a routine bone biopsy during PVP in treatment of "osteoporotic" vertebral fractures, was studied. A prospective follow-up study on the clinical outcome (Quality of Life as measured with the SF 36) up to 36 months after PVP for long-standing OVCFs, is discussed in **Chapter 4**. In **Chapter 5,** the clinical outcome of PVP in patients with long-standing OVCFs, treated with either low or medium viscosity PMMA bone cement, was evaluated in a prospective comparative follow-up study. In **Chapter 6,** a new system for **E**valuation and registration of e**X**tra vertebral cement leakage based on **A**natomy and **V**olume of the leakage using **CT**-scan analysis (the EXACT classification system), is proposed. Finally, in **Chapter 7** a review of the scientific evidence for PVP is presented.

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