

## Preoperative Motion-Related Pain in Cancer Patients with Extraspinal Metastases Treated by Percutaneous Osteoplasty

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### Abstract

**Purpose:** Percutaneous osteoplasty (POP) as a technical extension of percutaneous vertebroplasty (PVP) has been used as a treatment for painful extraspinal metastatic lesions besides the vertebrae. PVPs are performed in weight-bearing vertebrae; extraspinal POPs are usually performed in non-weight-bearing flat bones. Pain on extraspinal lesions may not be provoked by weight-bearing position but be provoked by specific motion. This study was performed to evaluate patient motion-related pain (MRP) and the resulting pain-related impairment (PRI) by specific motion according to the involved sites where extraspinal POP was performed.

**Methods:** We performed a retrospective study that evaluated the MRP and resultant PRI by reviewing the charts of 66 patients treated with 70 extraspinal POPs. The numeric rating scale (NRS) scores in 5 different positions including while lying on the back, lying on the affected side, sitting, standing, and walking and the Karnofsky performance scale (KPS) scores before and after POP were used to evaluate MRP and PRI, respectively.

**Results:** The postoperative mean NRS scores became significantly lower when patients were in specific 1 of the 5 positions: lying on their affected side following scapulothoracic osteoplasty; sitting following ischiothoracic osteoplasty; lying on their affected side in iliopsoas osteoplasty; and lying on their affected side following costovertebral osteoplasty. The mean KPS scores in all patients became higher after POP.

**Conclusions:** The characteristic preoperative MRP and the resulting PRI according to the involved sites in cancer patients with extraspinal metastases developed by specific motion and alleviated pain and impairment by POP, if the cancer did not involve the joints.

**Keywords:** Karnofsky performance status scale; Movement; Neoplasm metastases; Pain measurement; Vertebroplasty

### Introduction

Percutaneous vertebroplasty (PVP) was introduced in 1987 to treat painful vertebral lesions [1]. There are 5 types of bones found within the human body: long, short, flat, sesamoid, and irregular bones. Vertebrae are irregular bones and do not fall into any other category due to their non-uniform shape [2]. In recent years, it has become possible to safely apply bone cements to the flat bones, except in case of irregular bones such as vertebrae. The term percutaneous osteoplasty (POP) is more appropriate than PVP to describe cementoplasty of painful bone as it has a broader meaning [3].

It is important to decide whether to perform POP according to the results of patients' pain provocation tests, which are related to their movements and positions, or the imaging studies. POP has to be performed by focusing on the pain-related impairment (PRI) that is based on their life expectancy [4]. The typical pain pattern of osteolytic or osteoblastic metastatic vertebral compression fractures is provoked or aggravated pain in a weight bearing position such as, standing or sitting, rather than lying down. Furthermore, a typical sign is severe tenderness on the supraspinatus area of the involved vertebra [5]. The interventional physician is accustomed to deciding whether to perform PVP on the basis of the symptoms and signs of metastatic vertebral compression fracture. However, it is not well known when the POPs has to be performed on the basis of the symptoms and signs of various metastatic extraspinal fractures.

Not all osteolytic or osteoblastic metastatic compression fractures produce pain. It is possible that patients will not complain of pain, even if the bone fractures are widespread in the body. The acronym OPQRST has been suggested as a mnemonic for assessing each individual pain problem as follow: "O" is onset, "P" is provocative or palliative, "Q" is

quality or character, "R" is region or radiation, "S" is severity or intensity, and "T" is timing of pain (continuous or intermittent) [6]. According to patients' movement, the fractures from metastases provoke the unique pain. Therefore, the "P" (provocation) may be the most important factor among acronym "OPQRST" in the assessment of the patients for the assessment of patients with metastatic bone pain.

Hence, the purpose of this study was to evaluate motion-related pain (MRP) and the resulting PRI in patients with metastatic bone cancer according to the different sites of where extraspinal POP was performed.

### Materials and Methods

This study reviewed 70 cases of extraspinal POPs performed in patients with 66 patients from January 2001 to December 2010. The protocol was approved by the institutional review board of Pusan National University Hospital and Pusan National University Yangsan Hospital.

An informed consent about potential complications of scapulothoracic osteoplasty including nerve injury, pneumothorax, bleeding, wound

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infection, and embolism from the patient also taken. The patient was placed in the prone position on a radiolucent table with an inflatable adjustable pillow. After aseptic draping, an outline of the left scapula, including the medial border, inferior angle, and lateral border, were drawn on the skin under fluoroscopic guidance. An additional inner line was drawn to indicate osteolytic bone defects confirmed by preoperative plain film and computed tomography, and 3 tender points were marked on the scapula. The procedure was planned with 3 different directions of approach. Three 13-gauges, 10-cm long bone biopsy needles were simultaneously inserted from the 3 different entry points to fill the osteolytic lesion with bone cement under fluoroscopic guidance. The procedure was performed under conscious sedation with basic monitoring such as electrocardiography, pulse oximetry, and noninvasive blood pressure. Local anesthesia was provided with a total of 20 mL of 1% lidocaine and intravenous analgesia with 30 mg of ketolorac and 100 µg of fentanyl. After confirming needle placement and ensuring that there was no extravasation of contrast medium, the cement (polymethylmethacrylate, PMMA) was injected with withdrawal of the bone biopsy needles. To avoid suprascapular nerve damage, the C-arm was obliqued about 16° to the left and angled cephalo-caudad about 18°. The suprascapular notch lies at the 12-1 o'clock position [3].

For the costoplasty using 13-gauge, 10-cm long needles, and the informed consent was the same content of scapuloplasty. However, for the ischioplasty and ilioplasty using 11-gauge, 10-cm long needles, there was no need to take informed consent about pneumothorax. Other POPs, including ischioplasty, ilioplasty, and costoplasty, were also performed as the same manner only when osteolytic lesions were corresponded to the intractable tender point. We chose the shortest way to approach the osteolytic lesions from the skin in case of the pelvic and rib bones according to diagnostic imaging studies. In case of ilioplasty with a prone position, the needle was advanced from the superior posterior iliac spine, iliac crest, and anterior superior iliac spine to the targeted osteolytic lesions while considering curvature of the iliac fossa not to pierce the pelvic organs. If needed, bending of the straight needle was sometimes helpful to advance because of the curvature of the iliac fossa. In case of ischioplasty with a prone position, needle entry point was the ischial tuberosity (Figure 1).

Our retrospective study of patients who had received POP treatment because of extraspinal refractory pain evaluated the MRP and PRI from patients' charts. The MRP was assessed in 5 different positions during

the following activities of daily living (ADLs): (1) lying on the back, (2) lying on the affected side, (3) sitting, (4) standing, and (5) walking. The numeric rating scale (NRS, ranging from 0 to 10, with 0 being no pain at all and 10 being the worst pain imaginable) scores relating to MRP before and at 1 week after POP were checked in the 5 different positions. The changes in the mean NRS scores before and at 1 week after POP were also compared among the 5 different positions. The PRI scores, using the Karnofsky performance scale (KPS, from 100 to 0%: normal to dead), were compared before and at 1 week after POP.

Statistical analysis was performed using the SPSS ver. 12.0 for Windows software package (SPSS Inc., Chicago, IL). The values were calculated as mean ± standard deviation in cases of ilioplasty. The mean NRS scores in the 5 different positions during ADLs and the mean KPS scores before and after POP were analyzed using the paired t-test. The changes in the mean NRS scores between before and at 1 week after POP were analyzed using the ANOVA test for multiple comparisons. There was no need to analyze NRS and KPS scores for statistical significance in cases of scapuloplasty, ischioplasty, and costoplasty due to the limited of number of patients.

## Results

The mean age was 68.5 ± 11.3 years. The male/female ratio was 36/30. Two male patient received POP in the scapula body from metastatic lung cancers. Three male patients, 2 with metastatic hepatocellular carcinoma and 1 with prostatic cancer, received POP in the unilateral ischium. Fifty-nine patients, 29 men and 30 women, received 63 POPs in the ilium. Bilateral ilioplasties were performed in 4 patients. Cancers were originated from the lung, prostate, breast, uterine cervix, colon, and an unknown origin, with the number of patients being 35, 15, 5, 2, 1, and 1, respectively. Two male patients, with lung cancer, received POP on the posterior rib (Table 1).

In POP of the scapula body, the pain was severe while lying on the affected side and back. After POP, the lower NRS scores and higher KPS scores were observed. In the POP in the ischium, the mean NRS score while sitting before POP was the highest among the 5 different positions. After POP, the mean NRS scores decreased and the mean KPS score increased. A significant postoperative decrease in NRS scores in all 5 positions and increase in KPS scores was observed for the POP of the ilium. The difference in the mean NRS scores before and 1 week after POP while lying on the affected side was significant as compared to those of the other 4 positions (Table 2, Figure 2).

Fortunately, there were no complications related POPs such

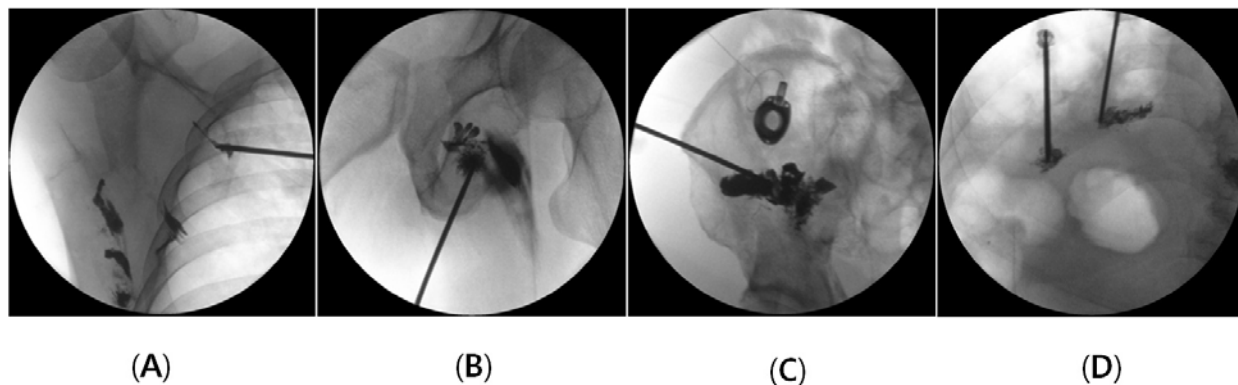


Figure 1: Percutaneous extraspinal osteoplasty. (A) Scapuloplasty, (B) Ischioplasty, (C) Ilioplasty, (D) Costoplasty.

Site of POP	Scapula	Ischium	Ilium	Rib
Number of patients who received POPs (M/F)	2/0	3/0	29/30	2/0
Primary origin of cancer metastases (Number of patients)	Lung (2)	Liver (2) Prostate (1)	Lung (35) Prostate (15) Breast (5) Uterine cervix (2) Colon (1) Unknown origin (1)	Lung (2)

Sixty six patients were treated with 70 extraspinal POPs including 4 bilateral ilioplasties.

**Table 1:** Demographic data and primary origin of cancer metastases according to site of percutaneous osteoplasty (POP) performed.

Specific Motion	Scapuloplasty	Ischioplasty	Ilioplasty	Costoplasty
Lying on the back	8.0 ± 1.0/1.0 ± 1.0	5.0 ± 1.0/0 ± 0.0	6.1 ± 1.2/1.2 ± 0.5*	7.5 ± 0.5/2.0 ± 0.0
Lying on the affected side	10.0 ± 0.0/2.0 ± 1.0†	6.3 ± 0.6/1.3 ± 0.6	8.6 ± 0.8/2.2 ± 0.8*†	9.5 ± 0.5/2.5 ± 0.5†
Sitting	6.0 ± 1.0/0.0 ± 0.0	9.7 ± 0.6/2.3 ± 0.6†	6.5 ± 2.1/1.9 ± 1.1*	4.5 ± 0.5/1.0 ± 0.0
Standing	5.0 ± 1.0/0.0 ± 0.0	5.0 ± 1.0/1.3 ± 0.6	4.5 ± 1.9/1.3 ± 0.3*	4.0 ± 1.0/1.0 ± 0.0
Walking	6.0 ± 1.0/0.0 ± 0.0	5.0 ± 1.0/0.0 ± 0.0	4.9 ± 1.6/0.5 ± 0.3*	5.5 ± 1.0/2.0 ± 0.0

Postoperative percutaneous (Post-POP) osteoplasty NRS scores were assessed 1 week after procedure. In cases of ilioplasties, values are expressed mean ± standard deviations.

\* P < 0.05. The decrease in NRS (scale, 0-10, with 0 being no pain at all and 10 being the worst pain imaginable) were significant between the before and 1 week after POPs.

† P < 0.05. The difference in mean NRS score before and at 1 week after POP while lying on the affected side was significant compared to those of the other 4 different positions.

**Table 2:** The numeric rating scale (NRS) scores according to specific motion in percutaneous osteoplasties (POPs).

as pneumothorax, cement embolism, nerve injury, organ damage, infection, or hematoma.

## Discussion

Each organ system possesses its own unique functions. For example, human skeletons have mechanical, synthetic, and metabolic functions. The mechanical functions are to protect internal organs, provide a frame to keep the body supported, move the body with the cooperation of skeletal muscles, tendons, ligaments, and joints, and hear the sound by transduction. The synthetic function refers to hematopoiesis, which occurs in the bone marrow. The metabolic functions are mineral storage such as calcium and phosphorus, growth factor storage, fat storage, acid-base balance, detoxification, and endocrine organ function [2]. If a bone loses its functions after fracture, this may lead to the development of pain, disability, and impairment. However, in the case of the primary function of the fractured bone, which is to protect the main organs, the occurrence of pain, disability, and impairment after fracture is related to specific motions.

The scapula, a large, flat, triangular bone, which partly overlaps with the second to seventh ribs on the posterolateral thoracic aspect. It has costal and dorsal surfaces; superior, lateral, and medial borders; inferior, superior, and lateral angles; and 3 processes known as the spinous, acromial, and coracoid processes. The lateral angle is truncated by the glenoid cavity for articulation with the humerus. This section, which is sometimes regarded as the head, is connected to the body by

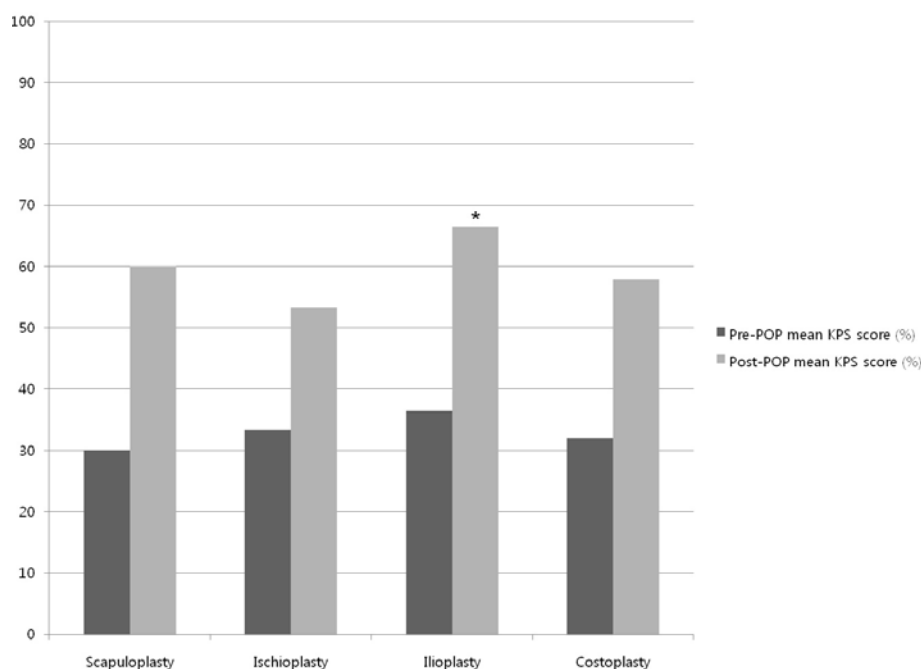
an inconspicuous neck [2]. Ordinary osteoplasties have been performed on load-bearing bones. The scapula was not previously considered an appropriate target for osteoplasty; however, in this case, the pain of the patient was provoked by lying on the back, especially while lying on the affected side, as well as by respiration in seated and standing positions. Although painful metastasis to the scapular body is rare, scapuloplasty may be minimally invasive option for preserving shoulder motion and alleviating intractable pain induced by lying on the back [3].

The pelvic girdle consists of 2 hip bones, which are connected anteriorly at each other at the pubic symphysis and posteriorly to the sacrum at the sacroiliac joints, thereby forming the pelvic ring. The hip is composed of the ilium, ischium, and pubis bones. The primary functions of the hip are to bear the weight of the upper body when sitting and standing, to transfer that weight from the axial skeleton to the lower appendicular skeleton when standing and walking, and to provide attachments for and withstand the forces of the powerful muscles involved in locomotion and posture. Compared to the shoulder girdle, the pelvic girdle is strong and rigid. Its secondary functions are to contain and protect the pelvic and abdominopelvic viscera [2]. The articular surface of the ilium (sacroiliac joint) and acetabulum, with each comprising two-fifth of the ilium and ischium, and one-fifth of the pubis (hip joint), are charged with bearing the weight of the upper body and transferring that weight from the axial skeleton to the lower appendicular skeleton. The remaining parts of the hip contain and protect the pelvic and abdominopelvic viscera. If various kinds of cancers metastasize to the hip that is not involved in these joints, pain, disability, and impairment may develop while sitting in the case of an ischial fracture and while lying on the back, especially while lying on the affected side in the case of an iliac fracture. It is not difficult to recognize the source of the relatively superficial somatic pain from both the active uptake observed in a bone scan and the additional severe tenderness around the fractured area.

It is not uncommon cases to perform costoplasty. The rib fractures due to osteolytic metastatic lesions are usually treated by radiofrequency ablation of the intercostal nerve after diagnostic nerve block. If not treated by neural ablation, the injection of alcohol into the lesion shows reasonable pain relief. However, in case of intractable pain from lying on the affected side, it is better to consider performing costoplasty.

The patients with a scapular body or an iliac fracture tend to sleep lying on the unaffected side and awaken from pain when lying on their affected side without intention. On contrary, the patients with an ischial fracture are frightened to sit on the affected side. The biggest treatment problem is how to place the bone cement adequately into the defects of curved flat bones. The answer is to understand the three-dimensional shape of the bone from the start. If an uncertainty remains, it is better to perform POP under computed tomogram rather than fluoroscope. A thinner needle, a 13-gauge rather than an 11-gauge, is recommended, as is curving the needle, if needed. If extraspinal POP is performed under fluoroscope, the needle location is frequently compared in the anteroposterior, oblique, and lateral views. If the needle is placed adequately on the target point, extravasation of the contrast media has to be confirmed before injecting the cement.

VPP of the axis (C2) is less aggressive than any surgical stabilizing procedure for the upper cervical spine, and it does not restrict the mobility of the upper cervical joints. Disruption of the weight-bearing unit of the second cervical body causes an excessive load at the relatively small adjacent upper cervical joints. To treat the mechanical component of the symptoms, anterolateral VPP at C2 was successfully performed, but the residual suboccipital headache was alleviated only after upper



**Figure 2:** The Karnofsky performance scale (KPS) score before and after percutaneous osteoplasty (POP). A significant postoperative increase in KPS scores was observed for the POP of the ilium (\*  $P < 0.05$ ). Other 3 kinds of POPs could not calculate for small candidates; however, they also showed significant postoperative increases in KPS.

cervical joint block was performed. Thus, upper cervical joint block can be performed to treat the residual suboccipital headache after PVP at C2 [7]. Other vertebral body fractures also disrupt the major weight-bearing unit; therefore, it is strongly recommended to evaluate for adjacent facet joint syndrome; and treat as needed [5]. In the case of non-weight bearing fractures, which are not related to joint motion, on the scapular body, iliac body and wing, and ischial tuberosity, ramus, and body, there is no additional burden from the new load. The pain provocation, disability, and impairment depend on the posture of the body. It is important to consider the pain provoking factors when painful patients scheduled for extraspinal POP.

Bone metastases pain has no correlation with site, extent and histological type of the primary tumor. The physiopathological mechanism of pain is based on the release of chemical agents by overturned bone and tumor cells, resulting in stimulation of endosteal nerves, inhibition of osteoblastic activity, periosteal stretching, pathological fractures, as well as infiltration and compression of nerve and surrounding tissues [8].

Possible mechanisms of pain relief following osteoplasty are alteration in response to mechanical, chemical, thermal, and vascular stimuli after injection of polymethyl methacrylate (PMMA). First, even minimal amounts of PMMA appear able to improve bone strength and load bearing. The improved stability and strength of the motion segment are hypothesized to reduce the pain stimulus. In addition, fracture reduction following vertebroplasty may result in the restoration of the anterior and posterior longitudinal ligament to a more favorable anatomical position, with a resulting decline in pain from pain afferents. Second, the PMMA monomer is an organic solvent. Exposure of tissue to the unreacted monomer is directly toxic to nerve endings with resulting in diminished pain perception. This may also explain, in part, the effectiveness of vertebroplasty in local tumor

control in terms of tumor necrosis. The ratio of monomer to powder during preparation, as well as the addition of an antibiotic, can affect the relative degree of tissue toxicity. Third, polymerization of PMMA is an exothermic reaction. Temperature as high as 50°C to 57°C have been recorded at the bone-cement interface during PMMA polymerization. Temperatures of 42°C to 47°C are sufficient to destroy several types of cells, including cartilage, embryonal tumors, carcinoma cells, and free nerve endings. Lastly, in addition, in cases of metastatic spinal disease, the elevated temperatures result in the destruction of tumor cells, and PMMA physically alters the vascular supply. Thermal injury, reduction of vascular supply to tumors, and direct tumor thermal injury are all possible mechanisms of pain relief following the use of PMMA [3]. However, PMMA cement still has a few shortcomings such as high modulus, hydrophobicity, and lack of bioactivity. Hydroxyapatite instead of PMMA may increase the bone cement's bioactivity; however, it is more expensive, and may show less thermal or chemical nerve ablation, and less direct tumor thermal injury effect [9].

Effectiveness of POPs related MRP and PRI was evaluated before and 1 week after POPs. It could be evaluated the results immediately after POPs. However, in case of outpatients or patients discharged from the hospital immediately after POPs, they were usually recommended to visit 1 week after POPs. At that time, they could describe their MRP and PRI exactly without pain at the insertion site and its related muscle strain.

Patients with metastatic tumor generally have short life expectancy and poor quality of life. Treatment is aimed at palliation and improvement of the performance status. The input of image-guided percutaneous ablation therapies with different ablative materials and techniques or POP also offer an alternative option for patients who are intolerant or unresponsive to standard treatments such as like radiotherapy and pharmacotherapy, yielding the benefit of

mininvasivity as well as prompt results, low adverse effects and shorter hospitalization stay [3,10].

It is difficult to find the results of studies related extrapural POPs in the treatment of painful bone metastatic cancers. The reasons are supposed that POPs have been introduced recently compared to PVPs, and extrapural metastases rather than spinal metastases are less frequent and painful. The number of studies of POPs is found quite small and the POPs are called as scapuloplasty, costoplasty, ischioplasty, and ilioplasty according to the performed sites. The POPs are also called as cementoplasty. An article related the efficacy and safety for percutaneous cementoplasty in the treatment of extrapural painful bone metastases was introduced recently [11]. They had performed POPs on the pelvic bones, tibia, femur, and humerus in 50 patients. The result was effective to obtain pain regression in painful bone metastases not responding to conventional analgesic therapy; bone consolidation could not be obtained in the diaphysis of long weight-bearing bones. There is a great difference in the sites of POPs from our study. They had performed POPs on the weight-bearing bones; however, we performed the non-weight bearing bones. The major provoking factor for pain was not a weight-bearing position, but a dependent position. They had performed radiofrequency ablation simultaneously; however, we performed radiofrequency ablation prior to POPs. The other report included POPs on the scapula and iliac bones. They also performed cementoplasty alone or in combination with radiofrequency ablation in 14 extrapural segments in 13 patients [12]. However, there was no concept about provoking and relieving factor for pain.

The limitation of this study is that in total, only 1 and 3 patient cases of POP in the scapular body and ischium respectively were included. However, the development of characteristic pain provocation, disability, and impairment according to a specific motion do not seem to change between the individual patients. In addition, lack of experience of POPs on other flat bones such as the skull, sternum, and rib may show their own specific MRP and PRI. There are few opportunities to perform POPs. The patients with skull metastases usually complain of headache due to increased intracranial hypertension, not pain on the skull. In cases of rib metastases, the pain is relieved by radiofrequency ablation of intercostal nerves.

In conclusion, the characteristic preoperative MRP and the resulting PRI according to the involved sites in cancer patients with extrapural metastases developed by specific motion and alleviated pain and impairment by POP, if the cancer did not involve the joints.

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