

**Basic Certificate in Palliative Care**  
**Dr. Geeta Joshi**  
**Dr. Piyush Gupta**  
**Dr. Col. Yashavant Joshi**  
**International Institute of Distance Learning**  
**Indian Institute of Technology, Kanpur**

**Week-07**  
**Lecture 02: Metastatic Bone Pain Management**

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**Management of**  
**Metastatic Bone Pain**

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Namaskar (Hindi word meaning greetings). Today, we are going to talk about the metastatic bone pain that means the pain which happens because of the bone metastasis that is the cancer pain. So, I am Dr. Anurag Agrawal presently working as pain physician and a professor of Anesthesiology at Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow, Uttar Pradesh, Bharat, India.

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## DR. ANURAG AGARWAL



- ▶ **Present Designation:** 'Pain-Spine Physician' & Prof.(Jr)
- ▶ **Place of Work:** Dr Ram Manohar Lohia Institute of Medical Institute, Lucknow U.P., India
- ▶ **Education:** M.B.B.S., M.D. (Anaesthesiology); P.D.C.C.- Pain Management (B.H.U.), F.I.A.P.M.
- ▶ **Publications:** 35 in National/ International Journals
- ▶ **Areas of Interest:** interventional Pain & Spine Management

I have done my MBBS and MD in Anesthesiology as well as PDCC in pain medicine from BHU that is Banaras Hindu University and I have interest in interventional pain and spine medicine and Percutaneous spine endoscopy. I am Vice President of NAPCAIM, UP chapter.

I am also the founder president of Endoscopic Spine and Interventional Pain Society. I have been secretary of Indian Society of Pain Clinicians and I am member of Pain Medicine Board of National Board of Examination of Medical Sciences in India that is NBEMS. I am also a member of Cancer Aid Society, Ethics Committee.

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## Incidence & Prevalence..

- Bone- third most common site of metastasis, behind lung and liver
- indicates a short-term prognosis
- median-survival from diagnosis of bone metastasis- 6-48 months
- majority of skeletal metastases are due to breast and prostate cancer (70%)
- much more common than primary bone cancers, especially in adults.

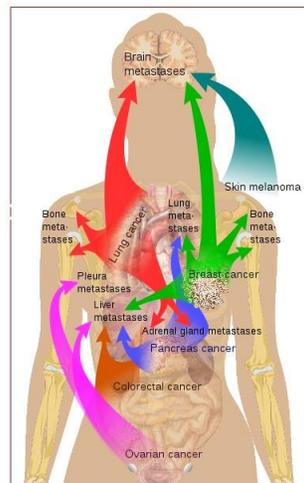
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So, the incidence and prevalence of bone metastatic pain that is very important to understand because until unless you know the magnitude of problem you cannot manage it.

So, bone is the third most common site of metastasis after lung and liver in all kind of cancers. It indicates a short term prognosis unfortunately. When a patient of cancer is having bone metastasis you can be sure that patient is not having too much of time. Medium survival from the diagnosis of bone metastasis in different studies and different stages of cancer patient is ranging 6 to 48 months. Majority of the skeletal metastasis are due to the breast and prostate cancer that the incidence goes up to 70 percent of patients.

And bone metastasis that is the secondary cancer lesion because primary some place else like in the prostate or in the breast. So, but the incidence of metastasis in the bones are much more common than the primary bone cancers.

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## Some Statistics

**70% ... Ca Prostate & Breast**  
**30% ... Lung, Bladder, Thyroid**  
**80% ... In axial skeleton**



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So, 70 percent of prostate cancer and breast cancer patients are likely to have bone metastasis while 30 percent of lung, bladder and thyroid cancer patients can also have bone metastasis. And in 80 percent of the patients who are having bone metastasis it is likely to be there in the axial skeleton. So, you please remember the axial skeleton the body is made up of skeleton the arm, the leg they are the peripheral skeleton like the humerus, femur they are the peripheral bone.

What is the axial skeleton that is the spine of the patients. So, consequence of this is severe bone pain, pathologic fractures, symptoms of hypercalcemia or it may cause spinal cord compression which results in the impaired mobility and deterioration quality of life. Patient is unable to walk, unable to sit or stand because of the vertebral metastasis we see day in and day out of those patients, increased medical cost and negative impact on the survival.

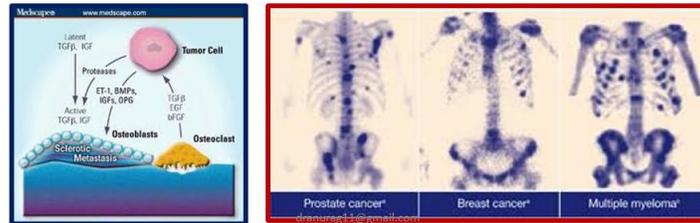
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## Types of Bone Metastasis

**Osteoclast:** bone destruction arises by the action of osteoclasts  
e.g. in patients with Breast cancer

**Osteoblast:** characterized by sclerosis  
e.g. in patients with Prostate cancer

**Mixed:** both resorption and formation occur simultaneously



So, type of bone metastasis they can be osteoclast, they can be osteoclast and they can be mixed where in the osteoclast there is a lytic activity that means, bone is getting dissolved by the osteoclastic activity. So, bone restriction arises by the action of osteoclast that happens in the breast cancer, but there can be another thing which there is increased formation of bone.

So, that is known as osteoblastic activity which is characterized by sclerosis it usually happens with the prostate cancer and then there can be condition where both osteoblastic as well as osteoclastic activities present in the same lesion. So, here you can see in the prostate cancer patient this is a bone scan picture where you can see increase sclerosis is a multiple level. So, here it is a lesion, here it is a lesion whole skeleton almost is full of metastasis.

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## Diagnosis of bone metastasis

- ❖ Localised pain, tenderness
- ❖ Detailed history
- ❖ Radiological imaging
- ❖ Radionuclide bone scan
- ❖ Biochemical markers
- ❖ Serum Alkaline phosphatase
- ❖ Procollagen terminal peptide
- ❖ Tumor markers :
  - PSA, prostate cancer
  - CA 27.29, CA 15.3 breast cancer



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So, how to diagnose the bone metastasis? And usually complaint of the localized pain and tenderness then there is history you need to take radiological imaging like they start with the X-ray here you can see there is the lytic lesion in the upper part of humerus. Then radionuclide bone scan may be required biological markers alkaline phosphatase, multiple blood test, multiple X-rays, MRI, CT scan they all are required to make a diagnosis and to provide a treatment.

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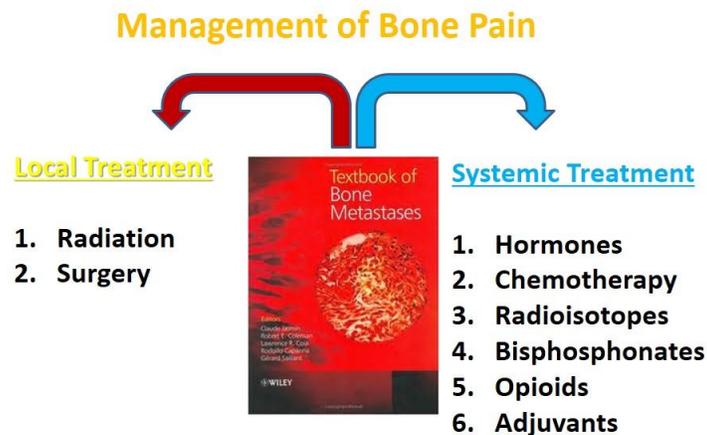
## Survival in Patients with Bone Mets

Disease	% Bone Mets	Type of Bone mets	5 yrs survival	Median survival
Cancer Breast	70%	Mixed Osteolytic >osteogenic	20%	24 months
Cancer Prostate	65 – 75%	Mixed >osteogenic Osteolytic	25%	40 months
Cancer Lung	30 – 40%	Mainly Osteolytic	Only 2 to 5%	< 6 months
Renal Cancer	25 – 30%	Mainly Osteolytic	----	< 9 months
Multiple myeloma	90 - 100%	Mainly Osteolytic	10 %	20 months

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So, as I told you survival is quite less in the cancer breast 70 percent patients are having bone mets and 5 year survival is only 20 percent and median survival is 24 months in the carcinoprostate 75 percent patients are having bone metastasis and most of the time 5 year survival is only 25 percent, but slightly more median survival that is up to 40 months then the cancer patient. Carcinoma lung very bad prognosis 40 percent are having bone metastasis mainly osteolytic and 5 year survival is only 2 to 5 percent. Same is the renal cancer multiple myeloma. Again very common up to 100 percent patients are coming with the bone metastatic and they are mainly osteolytic, but 5 year survival is only 10 percent.

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So, how to manage the bone pain due to the bone metastasis? You do the local treatment like the radiation or surgery if it is possible and then there is a systemic treatment where you use the multiple combination of drugs like the hormone, chemotherapy, radioisotope, bisphosphonate, opioids, adjuvants to treat this and then there is one treatment which is our niche as a pain physician that is minimally invasive pain and spine intervention MIPSIs like cementoplasty, like vertebroplasty, like kyphoplasty, like vertebral stenting system the latest treatment for to treat this condition. We will show you some cases about this.

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## Effects of Bone Metastasis

- major cause for morbidity, characterized by
  - severe pain,
  - impaired mobility,
  - pathologic fractures,
  - spinal cord compression,
  - bone marrow aplasia
  - Hypercalcemia (poor prognosis with a median survival of 10-12 weeks)

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So, the effect of bone metastasis is severe pain, impaired mobility, pathologic fracture, spinal cord compression, bone marrow aplasia, hypercalcemia and hypercalcemia specifically is a marker of poor prognosis with median survival of only 10 to 12 weeks that means 2 to 3 months only.

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## Types of bone metastasis

- **Osteolytic**-destruction of normal bone, causes- multiple myeloma (MM), renal cell carcinoma, melanoma, non-small cell lung cancer, non-hodgkin lymphoma, thyroid cancer
- **Osteoblastic** (or sclerotic)-characterized by deposition of new bone, in prostate cancer, carcinoid, small cell lung cancer, Hodgkin lymphoma or medulloblastoma.
- **Mixed**- if a patient has both osteolytic and osteoblastic lesions, present in BC, gastrointestinal cancers and squamous cancers.

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So, as I already told you osteolytic can be there, osteoblastic can be there and mixed can be there.

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## Characteristics

- Bone metastasis are almost always multiple and involve axial skeleton.
- Pathologic fractures occur in 10-30%
- most frequent fracture site-
  - proximal parts of the long bones (femur fractures most common).
  - Rib fractures
  - vertebral collapses

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So, bone metastasis are almost always multiple and involves the axial skeleton that is the spine in majority of the patient and pathological fractures happen up to 30 percent of patients and most frequent fracture site as proximal part of long bones like the femur and humerus and then it can be refracture or vertebral collapse as it happens with the Multiple myeloma patient.

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## Bone pain characteristics

- poorly localized,
- worse at night,
- not necessarily relieved with sleep or lying down
- back pain in a patient with cancer- with an abnormal spinal radiograph- a warning for possible spinal cord compression

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So, characteristics are of the pain that they are poorly localized, they are usually worse at night is a very important feature please ask your patient they are having more pain in the night that means you need to examine and investigate your patient.

Not necessarily lived with sleep or lying down, back pain in a patient with cancer with an abnormal spinal radiograph a warning from spinal cord complication compression.

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## Investigations

- complete blood-cell count to evaluate for anemia and myelosuppression;
- serum calcium, phosphorus,
- 25-hydroxyvitamin D,
- alkaline phosphatase,
- creatinine,
- thyroid-stimulating hormone, protein electrophoresis
- parathyroid hormone level to identify bone turnover and evaluate hypercalcemia

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So, please rule out to investigate you need to have complete blood count serum calcium phosphorus, vitamin D alkyne phosphates, creatinine. So, all these multiple test, but please remember if you are working in a primary care setup and you do not have an answer after getting all these investigation to your patient. So, please do not get them, please do not make patient spend their money whatever amount they have remained with. You please if you are suspecting and patient is not responding to your primary treatment and you are unable to provide advanced treatment please refer the patient as such to a nearby pain physician or a pain medicine facility.

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### **Investigations continued..**

- *Bone scintigraphy* is highly sensitive but usually has a low specificity.
- A plain radiography is very specific but sensitivity is low (44-50%)
- CT, MRI have good sensitivity & specificity
- PET scans- best sensitivity & specificity

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So, bone scintigraphy is that is the bone scan is a highly sensitive, but has a low specificity pain radiograph is very specific, but sensitivity is low.

So, CT and MRI has a good sensitivity and specificity and then there is a PET scan also which can be, but they should be employed only when you are thinking that you are able to provide some extra treatment after having the investigations of your choice. So, please do not advise the battery of investigation to your patient rather it is better to refer the patient to the appropriate facility.

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## Treatment Bone Metastasis

- Non-steroidal Anti-inflammatory Drugs
- second most commonly used drugs are opioids
- Corticosteroids
- Calcitonin
- Bisphosphonates
- Denosumab

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So, the treatment starts with the non-steroidal anti-inflammatory NSAIDs like the ibuprofen and the diclofenac sodium. Second most commonly used drugs are opioids and here in the bone metastatic pain NSAIDs are usually more effective than the opioid drugs please remember. Then corticosteroids, calcitonin which is a hormonal replacement, bisphosphonate drugs and injection denosumab that is a rankle inhibitor they have been found to be very useful for the management of cancer pain.

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## Treatment Bone Metastasis

- **Bisphosphonates**
  - standard treatment for tumour-induced hypercalcaemia
  - sclerotic lesions respond similarly to lytic metastases
  - should take a supplement containing calcium and vitamin D.
- **Denosumab**- 120 mg/ monthly S.C. route

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Then bisphosphonates are considered to be the standard treatment for tumor induced hypercalcemia and sclerotic lesions like it happens in the carcinoma prostate they respond equally to the lytic lesion with the bisphosphonate. But please do not remember to prescribe a calcium and vitamin D along with bisphosphonate. Then comes the injection Denosumab this is a new therapy slightly costlier, but it has been found to be quite useful in the management of cancer pain.

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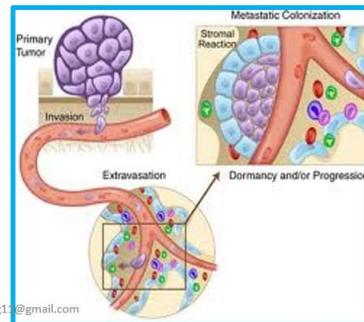
### Role of Bisphosphonates in Bone Mets

- **Binds to site of active bone metabolism**
- **Released from bone matrix during resorption**
- **Inhibit osteoclast activity**
- **Reduces Hypercalcemia & SRE, But pain-relief ???**
- **Used for Rx of Paget's disease, osteoporosis, Bone Mets**

**Zoledronic acid (2N<sub>2</sub>)**  
**4mg / 4 weeks / 15 mins**

#### **Caution**

Severe Renal impairment  
Children /Pregnancy  
Hypocalcemia  
Bronchial Asthma  
With NSAIDs



So, role of bisphosphonates in the bone metastatic binds to the site of its active bone metabolism. It is released from the bone matrix during the resorption and it inhibits the osteoplast activity.

It reduces the hypercalcemia and SRE, but pain relief is uncertain especially useful for the paget's disease, osteoporosis and bone metastasis. The most common preparation which is the IV preparation is being used is the zoledonic acid of bisphosphonate which is used in the 4 to 5 milligram per month in over 15 minutes.

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## Review of Literature

- ✓ There is evidence to support the effectiveness of bisphosphonates in providing some pain relief for bone metastases.
- ✓ There is insufficient evidence to recommend bisphosphonates for immediate effect; as first line therapy; to define the most effective bisphosphonates or their relative effectiveness for different primary neoplasms
- ✓ Bisphosphonates should be considered where analgesics and/or radiotherapy are inadequate for the management of painful bone metastases.

Wong RKS, Wiffen PJ. Bisphosphonates for the relief of pain secondary to bone metastases. Cochrane Database of Systematic Reviews 2002, Issue 2. Art. No.: CD002068

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So, there is evidence to support the use of bisphosphonates in providing some pain relief on bone metastasis, but there is insufficient evidence to recommend bisphosphonates for immediate relief as first line therapy.

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## Calcitonin in Bone Mets

- ✓ **Calcitonin used to treat metastatic bone pain**
- ✓ **Two studies fulfilled the selection criteria**
- ✓ **No evidence of Calcitonin effect ...**
  - **To control Complications of SRE**
  - **On improving quality of Life**
  - **On Patient survival**
- ✓ **Greater No. of Side Effects reported**

Martinez-Zapata MJ, et al. Calcitonin for metastatic bone pain. Cochrane Database of Systematic Reviews 2006, Issue 3. Art. No.: CD003223

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Calcitonin, calcitonin is used to treat the metastatic bone pain and few studies are there which fulfill the selection criteria. There is no evidence that calcitonin control the

complications of SRE, but there may be some pain relief which may lead to improving quality of life.

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## Radioisotopes for Bone Pain GCRI Experience

Isotope & Dose	Half Life	Response Rate	Onset of Pain relief	Duration	No of Patients
89Sr (4mci)	50.5 days	60-80 %	10-20 Days	2-12 mths	03
153Sm-EDTMP (8mci)	1.95 days	70-75 %	5-10 Days	2-6 mths	02
32P (60mci)	14.3	70-90%	5-14 Days	6 months	03

Limitations	Contraindications
Cost, License Used for disseminated disease Haematological Toxicity (32P) (< PC, Coag Profile) Delay in Onset	Myelosuppression Impaired renal function Spinal cord compression Impending bone fractures Life Expectancy ???

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Then comes the radio isotopes like the multiple isotopes this therapy has been given by the radiation oncologists. So, and most of these cancer patient they are under the treatment of either a radiation oncologist or a medical oncologist or a oncosurgeon. So, most of the time when the patient reach us in the pain medicine OPD these therapies already have been exhausted in most of the patient. So, there are multiple limitations which can be caused availability of high end machines then their contraindication when there is myelosuppression, renal function is impaired, spinal cord is compressed this these can be a contraindication.

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## Radiotherapy

- treatment of choice for localized bone pain,
- mechanism of pain relief after radiation therapy is poorly understood.
- If improvement in pain has not occurred by 6 weeks or more after treatment, it is unlikely to be achieved

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Then comes the radiotherapy for the choice of localized bone pain and then comes the mechanism of pain relief is poorly understood. If the improvement does not happen by the 6 week or more after the treatment it is likely to achieve radiotherapy has been done, but it is not working then it is not working going to work.

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### Radiotherapy for Painful Spinal Metastases

- mainstay of treatment

#### Limitations of Radiotherapy

Requires 2-6 weeks to take effect Patients

with limited life expectancy

Already reached maximum level of radiation

The Cancer Patient Fracture Evaluation (CAFE) trial was a randomized controlled trial at 22 sites in Europe, USA, Canada and Australia  
Cancer Control ;April 2012, Vol. 19, No. 2

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So, still it is considered to be the main stay of painful metastasis, but it usually take 2 to 4 weeks to take effect and it if after 6 weeks patient is not relieved it is unlikely to be relieved.

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## Other therapies

- **Radionuclide therapy** -systemic use of radioisotopes for bone pain.
  - Radiopharmaceuticals like strontium-89, rhenium-186 or samarium-153,
  - most effective for osteoblastic metastases
- **Radiofrequency & Cryo-ablation (RFA)**
- **Surgery** - only indicated for fractures of long bones and hip joints, in spinal cord involvement, or peripheral nerve compression.

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What are the other therapies like the radionuclide therapies like the samarium and other therapies for that you need to send them to a specialized center which is having a facility of nuclear medicine or radiation oncologists who are providing these therapies. Then comes the role of us as a pain physician that is radio frequency and cryo-ablation which are the minimally invasive and percutaneous therapies for the use in this patient. And surgeries only indicated when there is a obvious fracture of long bone and hip joint or there is a impending spinal cord involvement compression.

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## Percutaneous cementoplasty

- for bone metastatic lesions in the spine, pelvis, ilium, and proximal femur
- immediately restore the mechanical stability of affected bones,
- prevent further risk of bone fractures, and
- allow immediate weight bearing.
- emerging as one of the most promising procedures for patients with painful bone metastasis

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So, now there are few interventions which are very new, but very advanced and very effective till now as the literature and evidence supports. So, these are the therapies which we are providing at our pain medicine unit at Dr. Ram Manohar Lohia Institute of Medical Sciences Lucknow, Uttar Pradesh Bharat to our patients of bone metastatic pain. They are percutaneous cementoplasty common name is percutaneous cementoplasty. The aim is to fill the lesion of bone where the metastasis is there which is causing pain causing lysis or blastis and mixed type of lesion.

We go we fill it with the specialized bone cement that is PMMA and to decrease the chances of further fractures to decrease the pain and it works immediately. So, this is very important and good therapy to know about that is if the lesion is in the spine and it is not compressing the spinal cord pelvis, ilium or proximal femur or humerus this percutaneous cementoplasty can be used and it immediately restores the mechanical stability. It prevents further risk of bone fracture and allows immediate weight bearing. So, this is emerging as one of the most promising process for the patient with bone painful bone metastasis. The best part of our MIPS treatment that is minimally invasive pain and spine interventions of pain medicine is like it is like the cardiology like the angioplasty.

If you remember 20 years back most of the patient who were suffering from the heart disease used to undergo the bypass surgery, but now since last 15-20 years you know that most of these patients are being managed with the angiography followed by angioplasty if required. So, that is the same setup same thing which we are doing with our patients of chronic pain syndrome with the use of minimally invasive pain and spine intervention. They can be equated to the angioplasty and angiography where the benefit is that there is no big incision, there is no big or long term hospital stay, they are cost effective immediate return to the normal activity or life is permitted and with immediate results.

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### **Case 1- Metastasis in Distal Femur and Severe Knee Pain...**



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## Managed with Percutaneous Femoroplasty

- Immediate pain relief of more than 80%
- Full weight bearing after one week

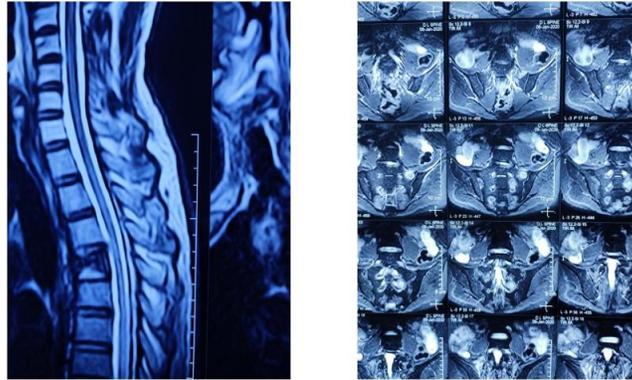


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So, here few cases of ours where you can see that there is a metastatic lesion in the bone and which was later on filled with the cement and patient got immediate relief here you can see this is the and what we do we did it a cementoplasty of the lower end of femur with the immediate pain relief of more than 80 percent and full weight wearing after 1 week and with the pencil rather pinhole incision no big incision nothing. So, that is known as femuroplasty.

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## Case 2- Ca Buccal Mucosa with # D4 & Left Sacral Ala Metastasis

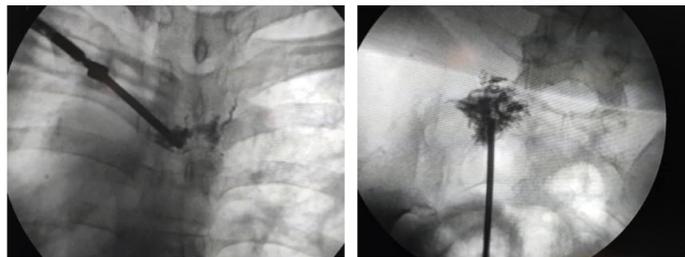


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Another patient he was a patient of carcinoma buccal mucosa oral cancer patient with fracture of D4 vertebra and sacral metastasis. Here you can see that this is the MRI picture of the patient's MRI and where you can see this vertebra is collapsed severely painful patient was unable to walk sit or lie down and then there was a lesion in the sacrum here you can see on the left side of sacrum. So, for because of these two lesions patient was enabled to sit down walk lying down even and patient was more in the night, pain was more in the night.

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## Percutaneous Vertebroplasty and Sacroplasty done with immediate pain relief..



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So, what we did we did we go and we did the percutaneous vertebroplasty and Sacroplasty where you can see our cannula is inside the collapse vertebra this black black is the PMMA bone cement and here also in the sacral part you can see this is the sacroplasty and immediate relief patient was walking after one week sitting together and patient was already under the active oncological treatment and we have the data of more than 5 years survival of this patient without any pain.

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**Case 3- Multiple Myeloma, with severe Back Pain & lesions in almost all Thoracic and Lumber Vertebrae... D11 and L1 lesions found to be painful..**



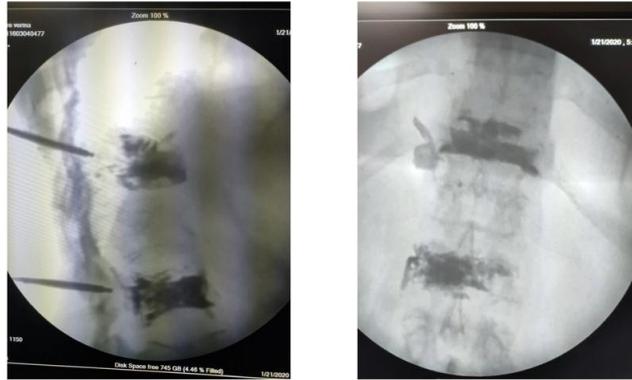
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Another patient multiple myeloma with severe back pain and lesions in almost all thoracic and lumbar vertebra D11 L1 lesions were found too painful.

This is the MRI of a multiple myeloma patient you can see the almost whole spine is being involved with the metastatic lesions especially there are two vertebra which are collars D11 and L1.

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## Percutaneous Vertebroplasty D11 and L1 lesions with Biopsy taken..



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Here on the x-ray also you can see that this D11 is collapsed this L1 is collapsed and what we did we did the vertebroplasty of both the lesion also took the biopsy where you can see a bone is filled with the cement bone cement and patient was immediately relieved.

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## MRI

Investigation of choice: Acute vs Chronic  
Extent of the disease; Epidural



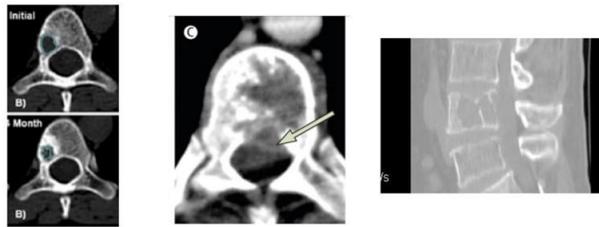
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So, the MRI is the investigation of choice if you want to do percutaneous cementoplasty verteoplasty of this patient because it is important to rule out that there is no spinal canal compression due to the spinal metastasis before you attempt these things.

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### CT Scan

- When MRI is contraindicated
- Suspicion of posterior cortex and pedicle involvement
- Osteolytic or osteoblastic lesion



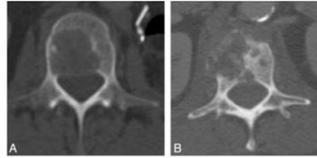
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When you have any doubt about the integrity of the bone please get a CT scan done. Like this patient is not our patient I cannot do a cementoplasty in this patient because this bone is completely destroyed. So, if I try to put cement in the collapse vertebra cement is likely to leak into the spinal canal and to compress the spinal cord which may result in the complication.

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## Contraindications for Cementoplasty

- Posterior cortical defect and pedicle involvement
- **Relative contraindication**
- Posterior cortical destruction- **Absolute contraindication**



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So, these are the contraindications of cementoplasty when there is a posterior cortical defect. So, that cement may leak into the canal we are not going to do it.

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## FB page & YouTube Channel for Pain Medicine awareness...



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So, this is my Facebook page with the name of Pain Free India Dr. Anurag Agarwal where we do multiple activities to increase the awareness about the available treatment and treatment option for the all kind of chronic pain syndrome. Be it cancer pain or non

cancer pain like the low back pain, joint pain, neuralgias, trigeminal neuralgias and multiple advanced treatment options.

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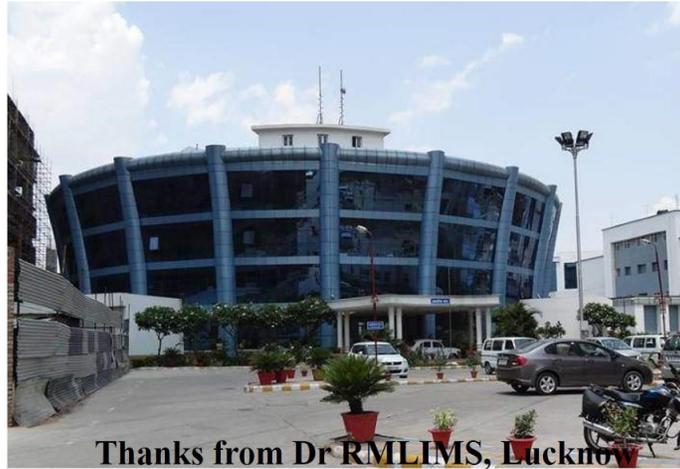
## FB page & YouTube Channel for Pain Medicine awareness...



And this is our YouTube channel with the name of Pain Free India Dr. Anurag Agarwal.

Again here we put the original videos for the interested pain physicians of the advanced interventions of MIPSIs which we provide to our patients as well as the testimonial videos to increase the awareness about the different chronic pain syndromes and their available treatment for the help of society because remember we want to make India Bharat a pain free India. So, that is our mission and motto of our life. There is a mail id and dranurag11@gmail.com and I have shown you my Facebook and YouTube channel please follow and subscribe and if you have any doubts any problem we are here to help.

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With this regards from the Dr. Ram Manohar Lohia institute this is my institute where I work at Lucknow, Uttar Pradesh Bharat. We are having a 1 year PDCC pain medicine course the eligibility is for the MD DNB anesthesiology. So, if you are interested and coming from the anesthesiology background and you are interested to join pain medicine to become a super specialist you can apply to our institute. You can also come for an observership of 1 to 3 months to our institute to see how we work what are the most advanced treatment options which can be done in the minimally invasive manner to help the patients of chronic pain syndrome. So, thank you all best wishes for your bright future and thank you.