

Radiofrequency Ablation of Bone Metastases

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Abstract: The purpose of this exhibit is to report our experience in radiofrequency ablation of bone metastases. Between January 1999 and January 2002, 68 patients with bone metastases were treated in our department. The technique, indications, and contraindications of radiofrequency ablation are described and illustrated. A wet mono- or bi-polar electrode is used for the ablation (Berchtold incl. Tuttlingen, Germany). The major indication is palliative treatment of bone metastases and pain management. However, curative ablation is performed in some special cases like bone metastases of thyroid cancer. In these cases, the treatment begins with radio frequency ablation with destruction of more than 90% of the lesion followed by 131- iodine therapy to complete the ablation of residual tumor. Complete necrosis was observed in 85% of cases. Radio-frequency ablation of bone metastases was promising in pain management with 78% of satisfactory results.

1) Introduction

Painful bone metastases commonly occur in advanced cancer patients. They are difficult to manage because of pain, reduction in mobility, and performance status. Possible mechanisms that may cause pain from bone metastases include the following:

- Stimulation of nerve endings in the endosteum resulting from the release of chemical agents from the destroyed bone tissue such as prostaglandins, bradykinin, substance P, or histamine;
- Stretching of periosteum by increasing size of the tumor;
- fractures;
- tumor growth into surrounding nerves and tissues.

Few of these mechanisms are supported by definitive data. Stimulation of nerve endings in the endosteum by chemical agents released from the destroyed bone tissue is probably the main cause of bone pain from small metastases; as metastases enlarge, stretching of the periosteum additionally contributes to the pain.

Traditional therapies to control pain and to treat bone metastases include the following:

- Radiation therapy
- Chemotherapy
- Hormonotherapy (prostate, breast)
- Analgesics
- And recently, pamidronate (biphosphonate) has been recognized as useful in osteolytic lesions.

These conventional therapies with the well known drawbacks and side effects provide reasonable pain relief obtaining variable success rates. Furthermore, radiotherapy and chemotherapy require a two to four week delay to reach efficiency.

In some cases, radiotherapy may not be an option because of radiation insensitivity of the tumor or high radiation doses previously delivered. Furthermore, chemotherapy may not be recommended because of its toxicity. Intolerable analgesic-related side effects may develop with increased doses.

Surgical resection is considered the only potentially curative option for secondary malignant bone tumors. However, in secondary bone tumors few patients are surgical candidates. Minimally invasive techniques with quick pain relief can be an alternative option to conventional treatments.

Several percutaneous procedures can be suggested:

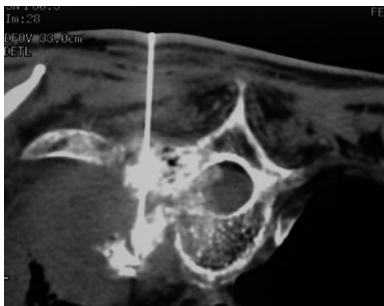
- Alcoholization,
- Cementoplasty (vertebroplasty, acetabular cementoplasty), and
- Thermal ablation:
 - Laser photocoagulation
 - Radiofrequency ablation

Radio-frequency (RF) ablation seems to be one of the most promising techniques consisting of thermal ablation of non-resectable tumors. In the following we will describe the use of radiofrequency (RF) ablation in bone metastases with the most suitable indications, the results, the advantages and the limits of this technique compared to the existing percutaneous interventions.

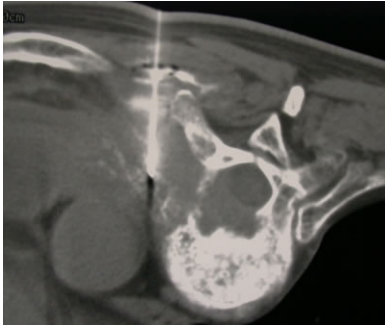
2) Percutaneous techniques

2.1 Alcoholization

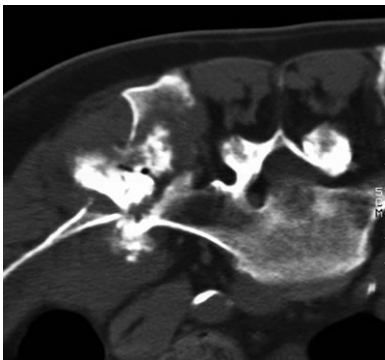
Percutaneous alcoholization of bone metastases is well suited in patients with painful severe osteolytic bone metastases if conventional anticancer therapy is ineffective and requires high doses of analgesics to control pain, and rapid pain relief is necessary. The major contraindication is the risk of ethanol diffusion into vital structures.



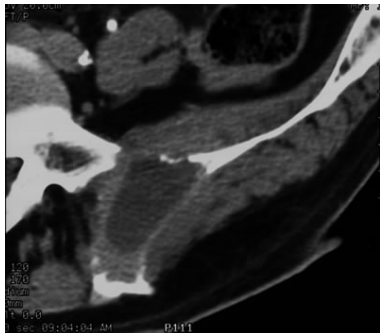
Bone metastasis alcoholization. Uneven distribution of the contrast and ethanol.



Spinal metastasis with paravertebral extension. Leakage of contrast along the needle tract. Risk of muscular and soft tissue necrosis.



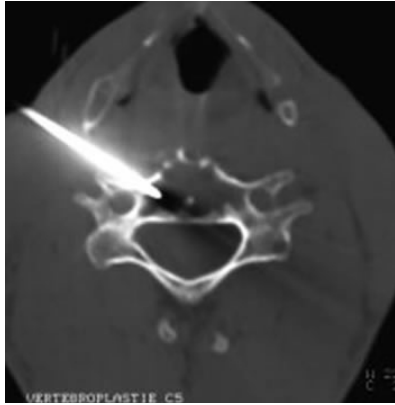
Painful iliac crest metastasis. Alcoholization with excellent pain relief. Note the uneven distribution of ethanol and an anterior leakage.



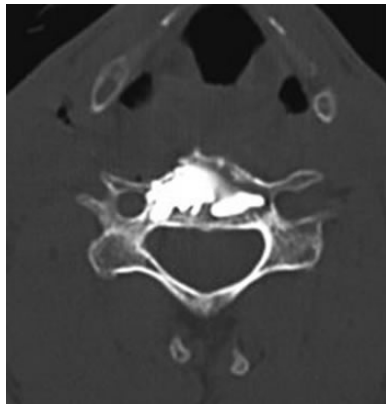
Large necrosis of the metastasis after alcoholization. Notable pain relief 12 hours after the procedure.

2.2 Cementoplasty

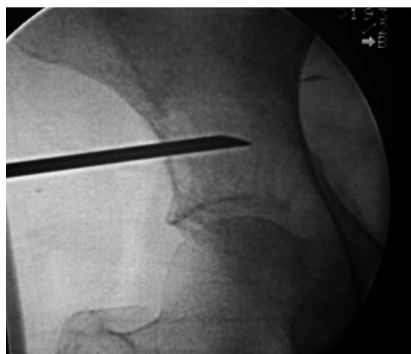
Painful spinal metastases are usually treated by a combination of vertebroplasty and radiotherapy. Vertebroplasty is an excellent palliative therapy with remarkable pain relief. However, vertebroplasty with injection of cement can be insufficient in pain reduction of spinal lesions with large paravertebral invasion. Injection of cement (cementoplasty) in other bone metastases locations (acetabulum) is possible. However, this technique is most suitable when both consolidation and pain management are required.



Cervical spine lesion treated with percutaneous vertebroplasty.



No leakage of cement. Vertebroplasty allows good consolidation and pain relief in this case.



Acetabular metastasis treated with percutaneous cementoplasty. The cement is injected inside the lytic lesion.

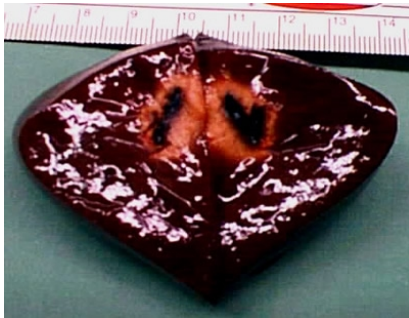


No leakage. Excellent pain relief. Cementoplasty allows consolidation and pain therapy in this case.

2.3 Thermal ablation

- Radio frequency (RF)
- Laser photocoagulation

The use of radio-frequency ablation was first reported in 1990 for the treatment of hepatic tumors. The size of the thermal coagulation produced by a single radio-frequency ablation is larger than that created by a single laser ablation.



Ex-vivo liver with coagulation produced by a single laser fiber. The lesion measures 15 to 20 mm diameter after 10 mn and 2 W of power.



In-vivo RF ablation with 50 W and 10 mn application. The lesion measures 4 cm of diameter.

3) Indications and Contraindications of RF ablation of bone metastases

The best indications of RF ablation of bone metastases are:

- Painful osteolytic bone metastases with or without soft tissue invasion
- Ablation of large bone metastases in thyroid cancer associated to radioisotope therapy (¹³¹iodine)

Radiofrequency is able to produce a much more predictable lesion than alcohol. This technique was first applied to tumor and pain management if alcoholization was contraindicated (risk of intra-articular leak, risk of accidental neurolysis).

Radiofrequency is an effective solution in sensitive regions because of the predictable size and well-shaped lesion produced by this technique. Furthermore there is no risk of leakage or collateral damage.

The distribution of alcohol is uneven within the tumor (particularly in large metastases). Either the needle has to be repositioned in regions of poor diffusion or multiple needles should be used. However, alcoholization is a relatively cost-effective technique.

In bone metastases with risk of pathological fracture, a consolidation method should complete RF ablation. For spinal and acetabular metastases, cementoplasty is an excellent alternative. In case of large invasion of soft tissue surrounding the vertebral body, RF ablation can be combined with vertebroplasty. However, the pain relief achieved by vertebroplasty and acetabular cementoplasty seems to be sufficient in lesions limited to vertebral body and acetabulum.

The usual contraindications are the same as the RF ablation of the liver. For the ablation of bone metastases, the monopolar technique (conventional RF) is contraindicated if the lesion is close to neurological structures or sensitive organs (colon, intestine). In these cases, the bipolar technique can be used for a precise limitation of the coagulation. Bone tumors consolidated with osteosynthesis should be avoided particularly when the electrode is close to metallic structures.



Painful osteolytic metastases are the best indications of RF ablation.

4) Mechanism of RF ablation

4.1) Monopolar RF ablation

Alternating electric current operated in the range of radio frequency can produce a focal thermal injury in living tissue. Shielded needle electrodes are used to concentrate the energy in selected tissues. The tip of the electrode conducts the current, which causes local ionic agitation and subsequent frictional heat, which leads to localized coagulation necrosis.

Basically, the term radio frequency refers not to the emitted wave but rather to the alternating electric current that oscillates in the range of high frequency (200-1,200 kHz). Schematically, a closed-loop circuit is created by placing a generator, a large dispersive electrode (ground pad), a patient, and a needle electrode in series.

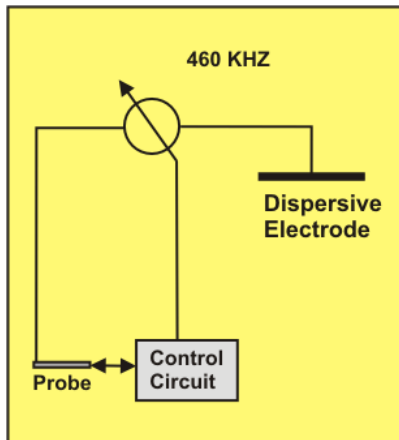
4.2) Bipolar RF ablation

With the bipolar technique, the dispersive electrode (ground pad) is replaced by a second electrode inserted parallel to the other electrode. In this way, the closed-loop circuit is created between the generator, the patient, and both electrodes. There is no loss of energy in the skin of the patient with deposition of the energy inside the lesion. The best results are obtained when the probes are parallel together and the tumor is limited in between. The distance between the electrodes is 3 to 4 cm maximum, 1 to 1.5 cm minimum. A different distance might be appropriate if probes with other geometries are used.

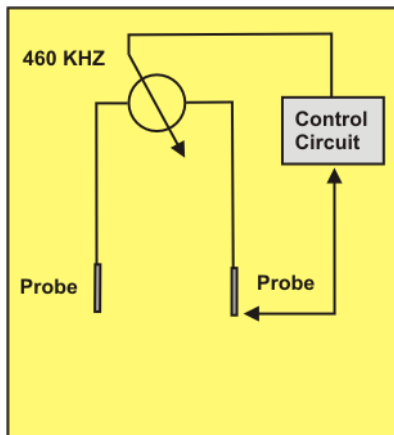
- Advantages of the bipolar technique: We propose a bipolar method for creating larger, faster and more controllable lesions.
 - The lesions are less dependent on local heterogeneity of the tissue such as blood perfusion and are strictly limited between the probes. The major contribution toward larger lesion size of bipolar ablation is based on a thermodynamic effect. Heat is trapped between the two probes and higher temperatures are reached. This results in a lesion of larger size than that of two lesions produced sequentially by monopolar ablation with probes placed at the same position.
 - The bipolar RF technique creates a cylindrical shaped lesion. Dependence of lesion size on local differences in cooling mediated by perfusion is reduced. This is supported by the fact that the standard deviation of bipolar ablation lesion size relative to its mean is smaller than for the monopolar case. Furthermore when a tumor is localized near sensible structures (Bowel, nerve root), the necrosis is well limited between the probes and accidental coagulation of the nearby organs can easily be avoided.
 - The proposed bipolar method reduces treatment time. The use of bipolar technique with a distance of 3 cm produces a well-limited coagulation between the electrodes with a maximum diameter of 4.3 cm plus/minus 0.5 cm after 5 to 10 minutes ex vivo.
- Drawbacks of the bipolar technique: the bipolar technique also introduces new drawbacks and difficulties:
 - The best results are obtained when the probes are parallel together and the tumor is limited in between. However Insertion of two parallel probes can be difficult in some cases. The ideal gap between the two probes depends upon the local properties of the

ablation site and is different for each ablation. We performed preliminary ex vivo experiments with probe distances of 4, 3.5, 3, and 2.5 cm. When the distance was 4 and 3.5 cm, in some cases we found a gap of viable tissue between two lesions created by the two probes after performing ablation. We chose a distance of 3 cm for subsequent experiments. A different distance might be appropriate if probes with other geometries are used.

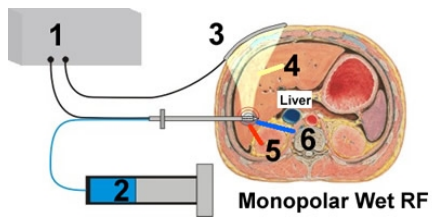
- Probe temperature can be different. In RF ablation, most of the active heating occurs within a range of a few millimeters from the electrodes. Similar resistivity and current density are present in the vicinity of both probes. Therefore, a comparable amount of energy is converted into heat next to each of the two probes. If one probe is cooled more by blood perfusion than the other, more heat energy is carried away. One probe can therefore reach a higher temperature than the other. This can lead to boiling and vaporization. Impedance will rise, and the RF generator shuts down. In 5 patients, during bipolar ablation the impedance showed a sudden rise resulting in the shutdown of the generator. In these cases, we used the temperature-controlled method. If the temperature of the hotter probe is controlled to be kept at 95 °C, the other probe will not reach this temperature and heating near this probe will be kept lower.
- Another drawback of the wet electrode is the risk of diffusion of hot saline. This risk can be decreased with the reduction of the volume of fluid injected by using hypertonic saline (5.85%). Using this method reduces the amount of saline injected.



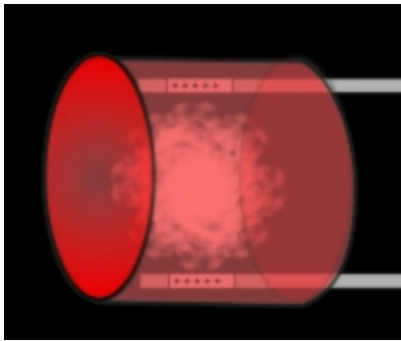
Monopolar RF



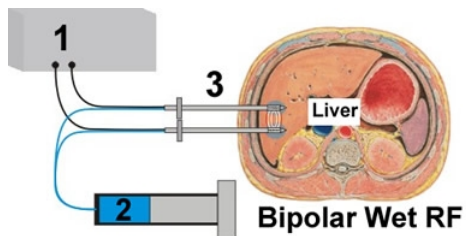
Bipolar RF



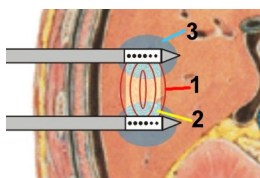
1. RF generator.
2. Continuous saline infusion.
3. Dispersive electrode (ground pad).
4. Closed loop.
5. Heating.
6. Saline infusion.



Bipolar RF. The bipolar RF technique creates a cylindrical shaped lesion (red) around the tumor.



1. RF generator.
2. Continuous saline infusion.
3. Bipolar needle electrodes inserted parallel together.



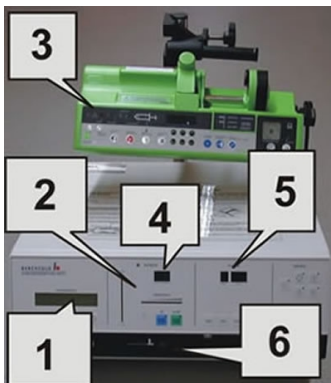
- 1. Heating.**
- 2. Closed loop between the electrodes.**
- 3. Continuous infusion of saline.**

5) Equipment for RF ablation

Each radio-frequency device consists of an electrical generator, needle electrode, and ground pad. Each manufacturer has a different needle electrode design. We are using a new commercially available device using a single probe system (18- to 16-gauge) with continuous infusion of saline without exceeding a 110°C maximum temperature threshold (60W, Berchtold®/ Tuttlingen, Germany). The continuous infusion of saline at the tip of the needle allows increasing heat and electrical conductivity. The Berchtold® radio frequency device relies on an electrical measurement of tissue impedance to determine that tissue boiling is taking place. Impedance increases can be detected by the generator, which can then reduce the current output and increase the saline flow. Injection of hypertonic saline during RF ablation can increase energy deposition, tissue heating, and induced coagulation.



Radio-frequency device with injection of continuous saline. The same generator is used for bipolar technique.



- 1. Monitor of Energy and temperature.**
- 2. Impedance control.**
- 3. Injector for continuous injection of saline.**
- 4. Power.**
- 5. Timing.**
- 6. Needle electrode input.**

6) Procedure

Radiofrequency technique is widely used in liver tumors. In our department we are using an electrode with continuous saline infusion to increase the coagulation size (Berchtold®, Tuttlingen, Germany). The infused electrode of 18 to 16 gauges is inserted inside the tumor and a power of 40 to 50 Watts is used for 10 minutes with continuous infusion of hypertonic saline 5.85% (56 to 62 ml/hour).

The advantages of hypertonic saline are the increase of electrical conductivity and reduction of the fluid volume injected. For large lesions ($\geq 4\text{cm}$), the procedure should be repeated after repositioning the needle electrode.

The guidance system is chosen based on operator preference and experience. We are using CT guidance on a routine basis for bone tumor ablations.

However MRI can be used for the needle insertion with thermal monitoring during ablation.

If a penetration of a thick bone is required, a coaxial technique should be applied for the insertion of the needle electrode. However, the coaxial technique using a bone biopsy needle should be handled with care because the bone needles are not insulated and the active part of the electrode should not be in contact with these needles in order to avoid loss of energy and coagulation of the needle tract.

With conventional monopolar technique, dispersive grounding pad was typically attached to the patients as close as possible to the needle electrode. In order to ensure that there is no interference with the heart rate, the heart should not be between the ground pad and the needle electrode.

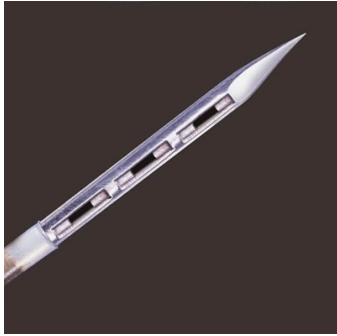
For spinal metastases or lesions too close to sensitive organs (nerve root, cord, colon, etc.) a specific bipolar technique was used inserting two electrodes in tandem. The major advantage of this bipolar system is that the coagulation is strictly limited between the electrodes. In this way, the adjacent organs are protected. Another advantage of bipolar technique is the fast coagulation of the area between the electrodes (approx. 5 minutes).

With bipolar technique the ground pad electrode is not necessary. The limitation of bipolar radiofrequency is the distance between the electrodes which is limited to a maximum of 3 to 4 cm. Furthermore, the bipolar procedure requires the use of two needle electrodes.

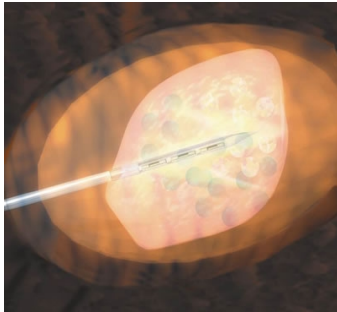
The number of ablations performed varied for each patient and depended on size, shape, origin, and location of the metastatic lesion. The duration of a procedure depends on the number of ablations to be performed.

Curative ablation is limited to some specific indications. Thyroid cancer metastases are a typical example. RF ablation is performed in this indication to reduce tumor size and is followed by 131-iodine therapy to complete the ablation of residual tumor.

The RF ablation of bone is painful and the procedure should be performed under general anesthesia or regional anesthesia. To avoid post procedural pain, injection of 10 ml of ropivacain 0.2 % in subperiosteal area is very useful with an analgesic effect of up to 12 hours.



Needle electrode (16-gauge) with continuous infusion of saline around the tip.



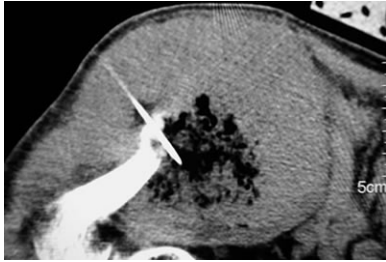
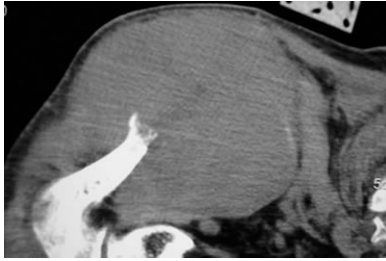
Needle electrode with continuous infusion of saline.



Interventional CT room.

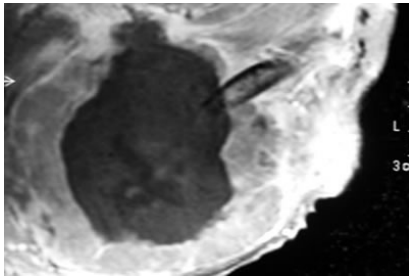


Patient installation with ground pads inserted close to the lesion.

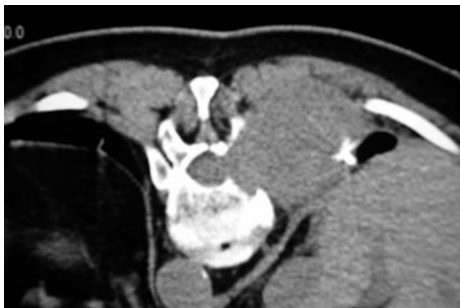


Large painful lytic metastasis.

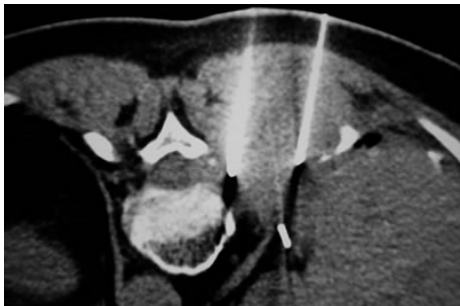
RF ablation of the metastasis with monopolar technique.



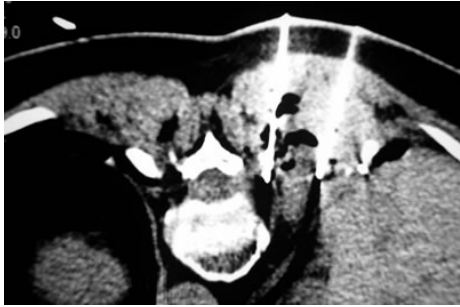
MR imaging 10 days after the RF ablation. Large but incomplete necrosis of the tumor.



Painful paravertebral metastasis.



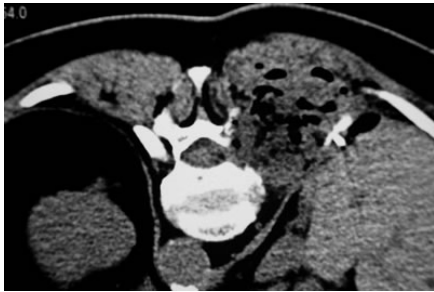
Bipolar technique to avoid neurological complications.



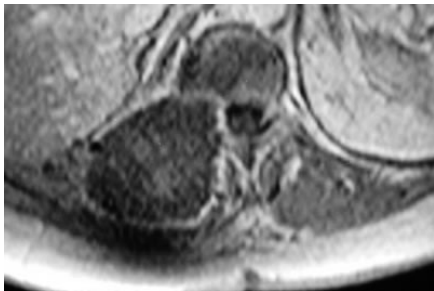
CT scan during RF ablation. Ablation between the electrodes. Coagulation outside the electrodes limited to 5 mm maximum. RF ablation duration 5 minutes per position.



The electrodes are repositioned and another 5 minutes RF ablation is performed.



CT scan after the procedure.



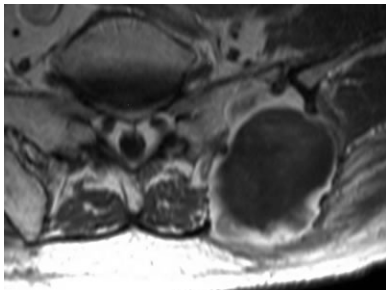
MR imaging (T1-weighted + gadolinium). Large necrosis of the tumor. No complications. Excellent pain relief.



View of the bipolar needle insertion with continuous infusion of saline.



Thyroid cancer metastasis treated by the association of RF ablation followed by radioisotope therapy.



Large necrosis of the tumor. After tumor reduction, residual lesions are treated by radioisotope therapy.



Installation of the patient for RF ablation under general anesthesia. Regional anesthesia can be used too.

7) Results

Between January 1999 and January 2002, 68 patients with painful osteolytic bone metastases were treated by RF ablation in our department. Nine thyroid cancer patients with metastatic bone lesions were treated by the combination of RF ablation and radioisotope therapy (Iodine 131). All treated lesions were osteolytic, including: lung carcinoma, breast carcinoma, thyroid carcinoma, renal cell carcinoma, colorectal carcinoma, melanoma, endometrial carcinoma.

Prior to RF ablation, each patient was assessed by using a validated visual-analogue scale for pain evaluation, and the use of analgesic medicine was recorded. A complete blood count and prothrombin time were obtained within 24 hours of the procedure. If no previous histologic or cytologic proof of the patient's malignancy had been obtained, a percutaneous biopsy was performed prior to treatment.

All patients underwent physical examination and a CT and MR imaging (maximum 2 weeks before the procedure) prior to treatment. With the monopolar technique, the coagulation size with a single energy delivery is about 40 mm in diameter. The coagulation with bipolar technique is strictly limited between the electrodes achieving a maximum of 3 to 4 cm.

The first follow-up is performed 7 to 10 days after the procedure with an MR examination to evaluate the necrosis. The procedure is repeated if the ablation is not complete and/or there is insufficient pain relief. Large bone metastases require multiple RF applications. If necessary, the procedure can be repeated every week.

In one patient with femoral metastasis, the laser photocoagulation was preferred to RF ablation due to the presence of a centromedullar osteosynthetic material.

During the first hours (12- 24 hours) after the procedure pain should be controlled by analgesics. Fever is systematic after a large necrosis. The septic risk is reduced by strict sterility.

Neurological complications are avoided by a precise anatomical knowledge of the treated region and precise CT guidance. No major complications in patients treated in our department have been reported. Careful selection of lesions, electrode placement, and use of bipolar technique are crucial to avoid inadvertent ablation of critical structures such as spinal cord, major nerves, bowel, and bladder.

In one case, along with the necrosis of the metastasis, there was also to a muscular necrosis with major pain for one week. The use of the bipolar technique with limitation of necrosis between the electrodes is very promising in these cases.

In bone metastases, 75% of resections were incomplete. Radio-frequency ablation of bone metastases was promising in pain management with **78% satisfactory results**.

One of the major advantages of the RF ablation of bone metastases is the quick pain relief occurring within 24 to 48 hours.

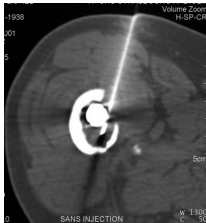
The mechanism of action responsible for decreased pain at the metastatic site after RF ablation is unclear. Several possible mechanisms responsible for decreased pain include:

- mechanical decompression of tumor volume, decreasing stimulation of sensory nerve fibers;
- destruction of tumor cells that produce nerve-stimulating cytokines (tumor necrosis factor, interleukins, and others), which may sensitize nerve fibers and affect pain transmission;
- physical destruction of adjacent sensory nerve fibers involving the periosteum and cortex of bone, inhibiting pain transmission; and
- inhibition of osteoclast activity, which may cause pain.

The best ablations were obtained in large metastases of thyroid cancer. As a matter of fact, the treatment has been performed in two steps. Initially, the radio frequency ablation was performed with destruction of more than 90% of the lesion followed by ¹³¹-iodine therapy to complete the ablation of residual tumor. Complete necrosis was observed in 85% of these cases.



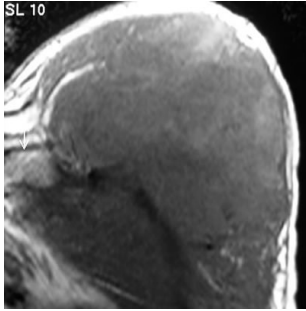
Large painful osteolytic metastasis. The lesion was consolidated previously by osteosynthesis. First, alcoholization was considered. Injection of contrast medium demonstrates a venous leakage. RF ablation was not possible because of the metallic material.



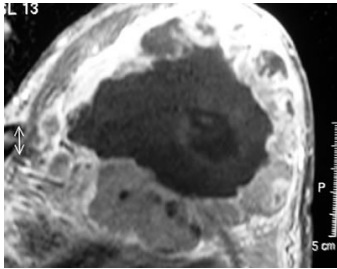
Laser photocoagulation was the only alternative.



Insertion of four 18-gauge spinal needle inside the lesion with coaxial insertion of the laser fibres. Simultaneous laser energy delivery through the needles for 10 minutes. Notable pain relief was obtained.



We used MR imaging in the evaluation of tumor before and after the RF ablation.



T1-weighted images with injection of gadolinium was useful in the appreciation of the necrosis. MR imaging was performed 10 days and 6 months after the procedures. The ablation zone appeared hypointense and non-enhancing.

8) Discussion



Approximately 40% of cancer patients develop metastatic disease; 50% of these patients have poorly controlled pain.

Various therapies, including chemotherapy, hormonal therapy, localized irradiation, systemic radioisotope therapy, biphosphonate therapy, and surgery, may be used in an attempt to provide palliative pain relief.

Some patients fail to derive satisfactory pain relief with these therapies, and relief, when achieved, may not occur until 4–12 weeks after the initiation of the treatment. When these methods are not possible or are not effective, analgesic medications remain as the only current alternative therapy.

The main advantage of radio-frequency ablation is the ability to create a well-controlled focal thermal injury with minimal morbidity and mortality.

Unlike alcoholization (ethanol ablation), radio-frequency ablation creates a well-demarcated lesion. The bipolar technique is able to create a strictly limited coagulation between the electrodes and the duration of the ablation is relatively short.

Radiofrequency is particularly indicated for tumor therapy. While alcoholization is preferred in palliative bone metastases pain management because of its simplicity and low cost. However, the risk of leakage, collateral damage, necessity of multiple needle insertions, and the uneven distribution of ethanol are major limits with this technique.

The size of the thermal injury created by a single radio-frequency ablation is larger than that created by a single laser ablation; hence, there is less chance of missing large tumor.

The management of patients with bone metastases requires consideration of many factors:

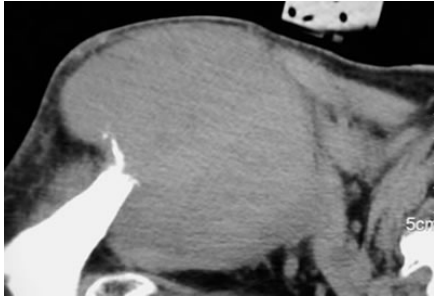
- careful evaluation of the patient's general condition,
- an understanding of the disease process,
- an appreciation of the degree of bone destruction (consolidation),
- and working knowledge of available treatment options is required.

A factor of concern with RF ablation is the time currently necessary for the RF ablation treatment, particularly for large lesions (multiple applications necessary). These treatments require an average of 2 hours of anesthesia time with the patient in the CT suite; a substantial component of the time necessary for the procedure was an average of 40 minutes of ablation time. Optimization of RF electrode energy deposition especially with bipolar technique may allow a decrease in the amount of time necessary for this procedure. In the evaluation of this technique the cost should also be taken into account.

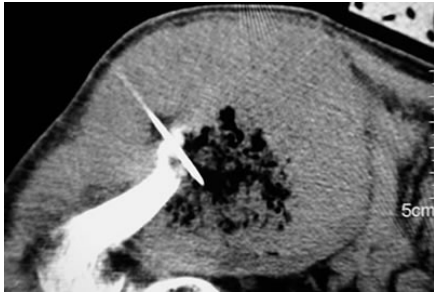
10) Cases

CASE 1 : 56-year-old man with a painful large scapular metastasis due to a lung cancer.

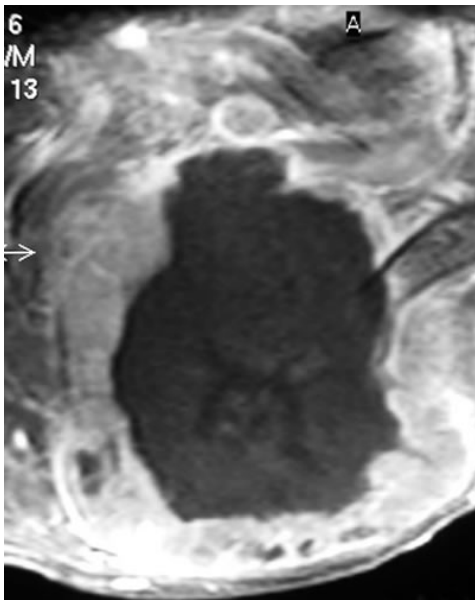




The ground pad is inserted close to the lesion.

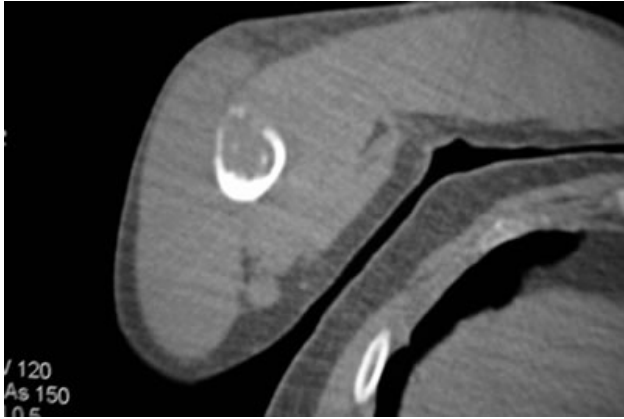


40 minutes of monopolar RF energy was delivered to the lesion with continuous infusion of hypertonic saline.



MR imaging demonstrates large but incomplete necrosis of the tumor after RF ablation.

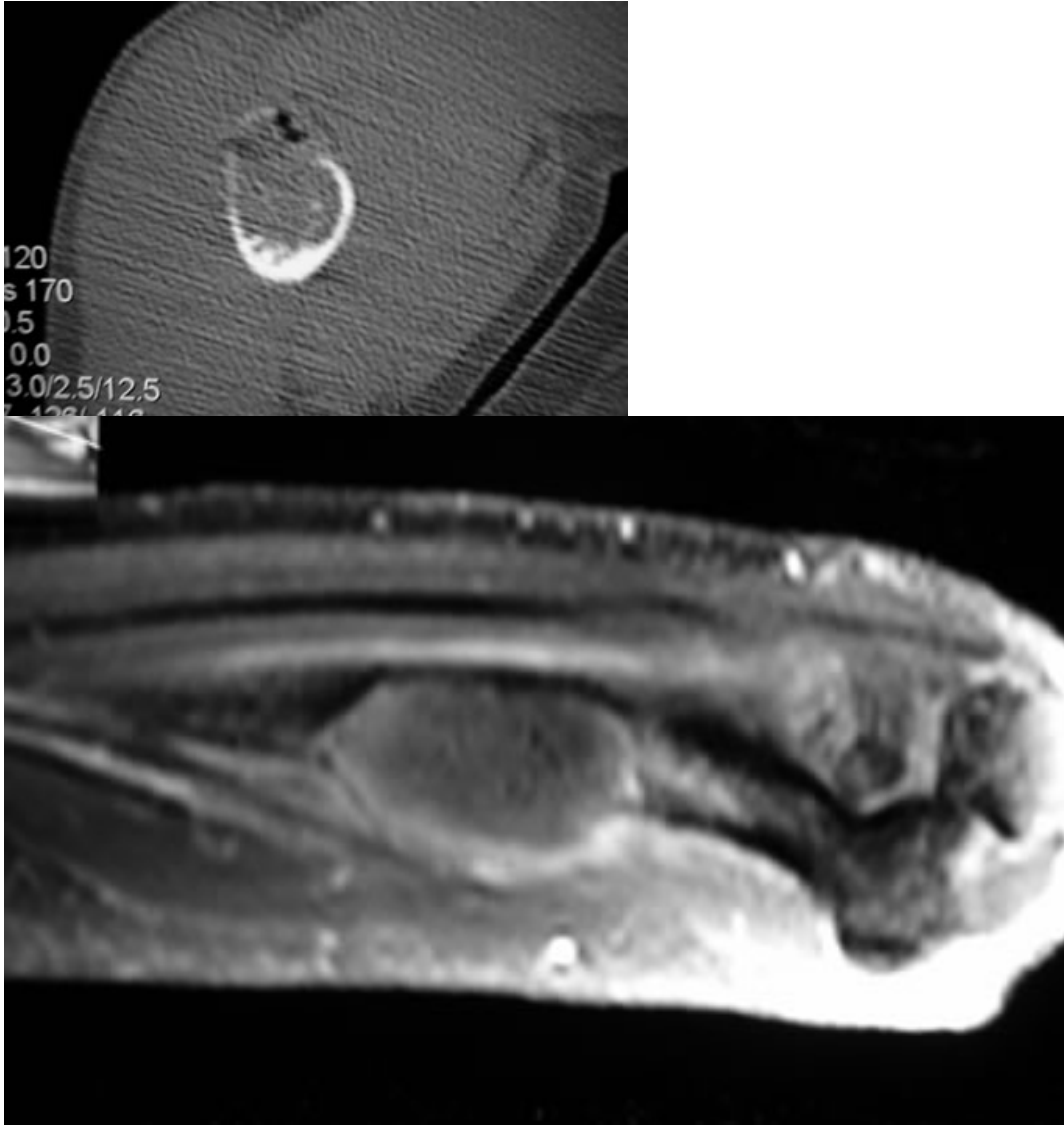
CASE 2



Extremely painful osteolytic humeral metastasis.



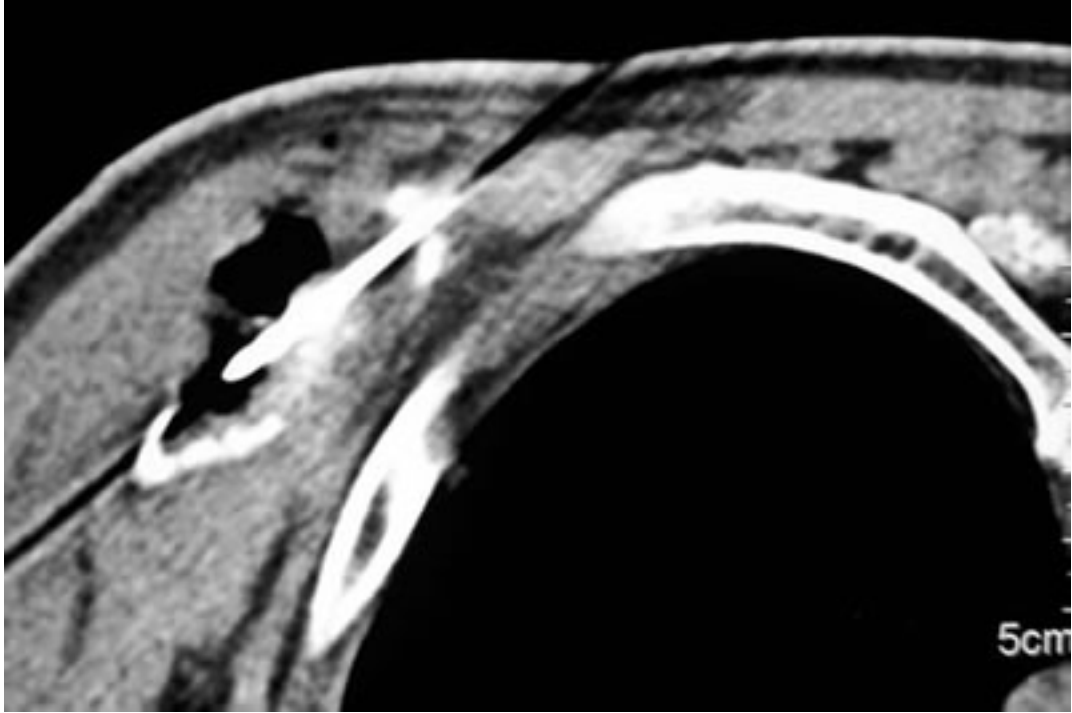
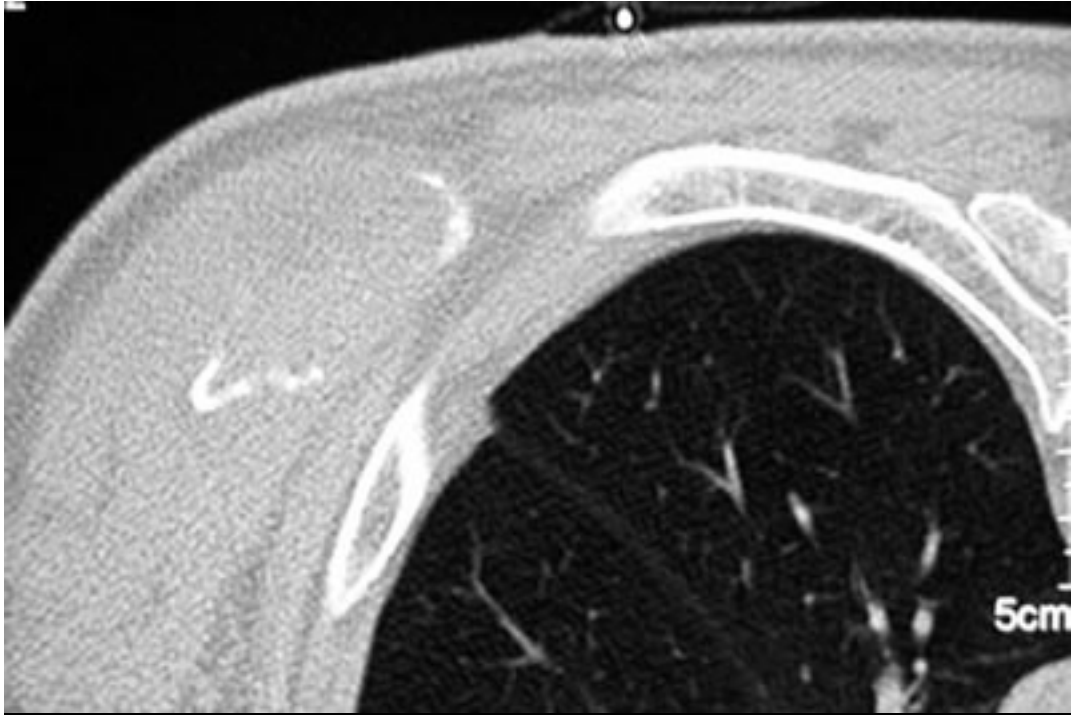
The needle electrode is inserted in the osteolytic lesion. RF ablation for 10 minutes (50 W and 62 ml/hours of 5.85% hypertonic saline infusion).

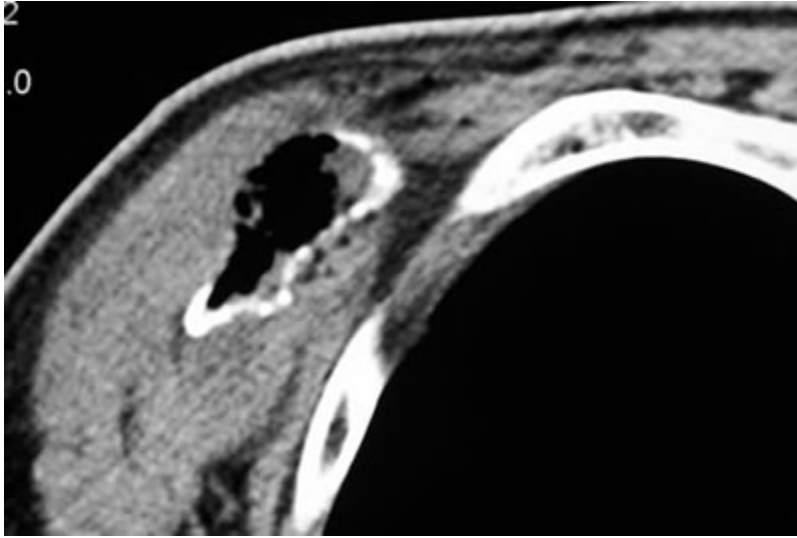


Large necrosis after RF ablation. Pain relief 48 hours after RF ablation.

CASE 3

Lung cancer patient with a painful scapular metastasis. RF ablation with excellent pain relief.





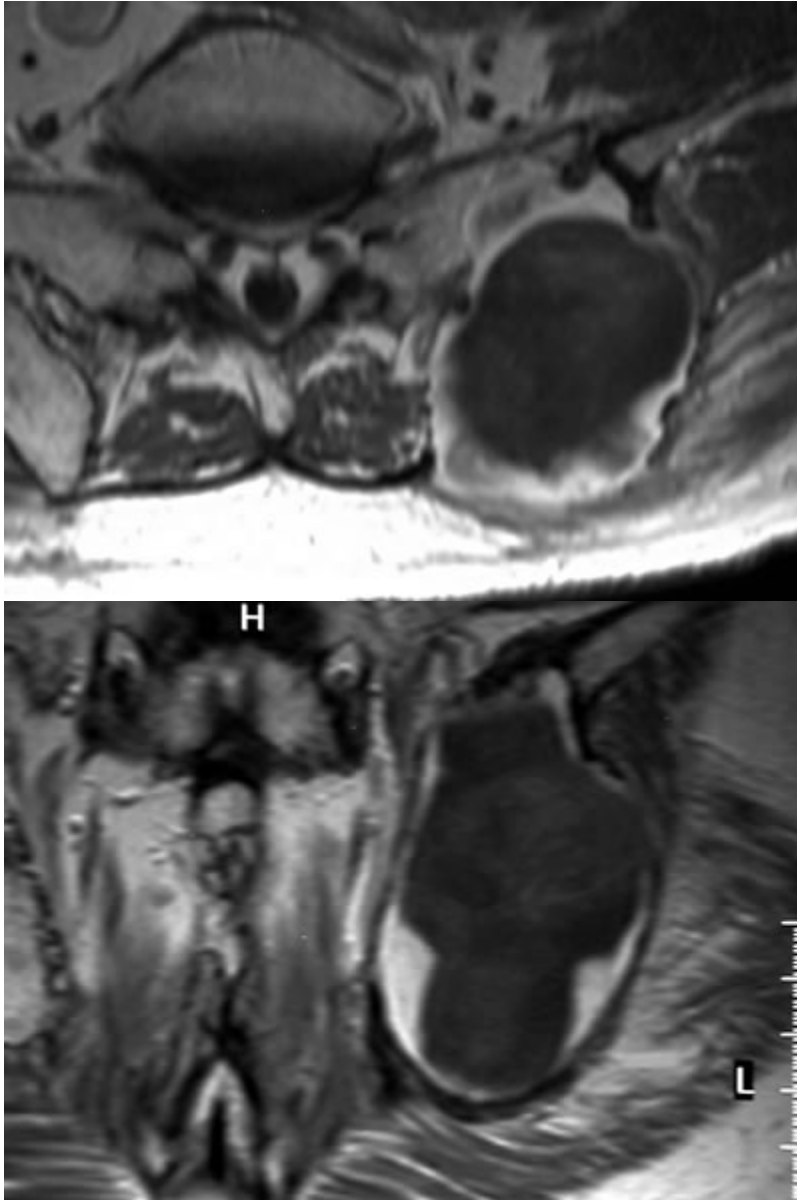
RF ablation with a single session of 8 minutes. Complete pain relief after 24 hours.

CASE 4

Thyroid cancer with large metastasis. The lesion is too large to be treated with radioisotope. Association of RF ablation and radioisotope therapy.





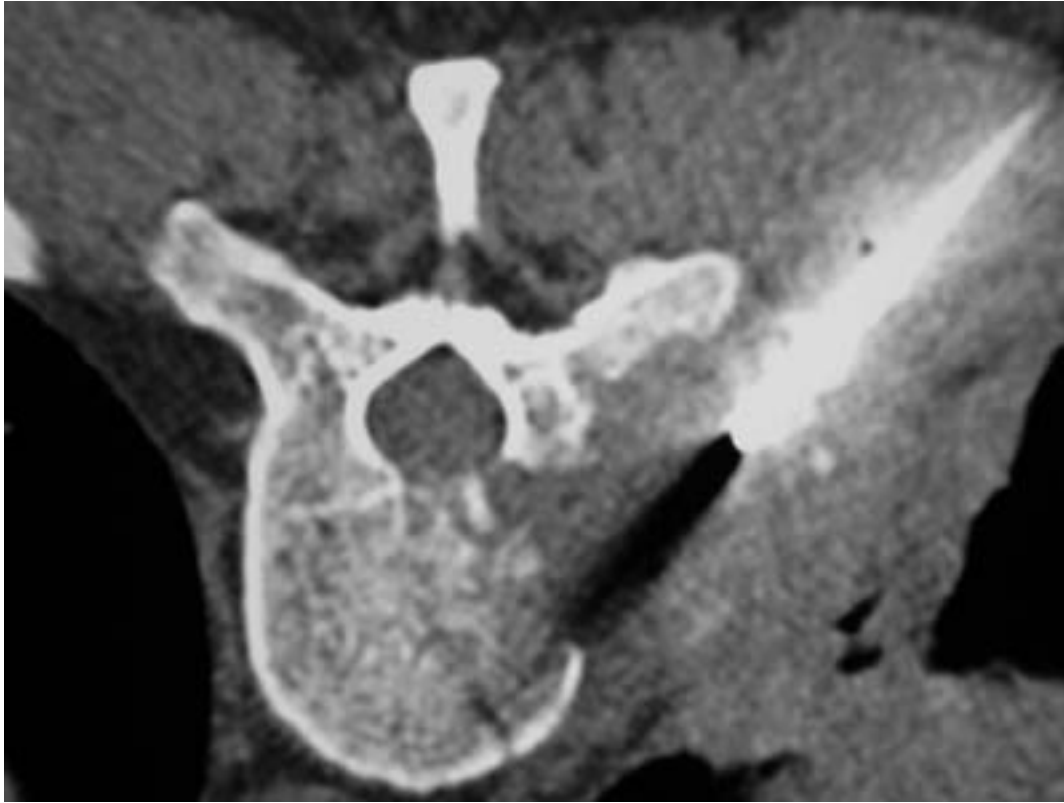


RF ablation reduces the lesion first and the rest of the tumor is treated with radioisotope therapy (Iodine 131).

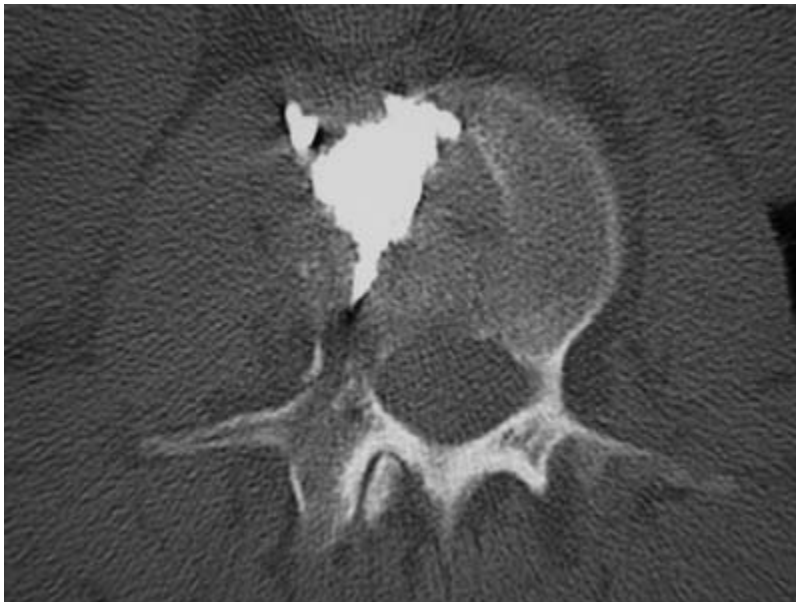
CASE 5

Painful spinal metastases. The lesion with large paravertebral extension was treated with RF ablation. The second painful metastasis was limited to the vertebral body and was treated successfully with vertebroplasty.





The RF electrode was placed in 3 different positions to increase the coagulation size.



The osteolytic metastasis limited to the right hemivertebra was treated by vertebroplasty. An excellent pain relief was obtained in this patient with the association of RF ablation and vertebroplasty.

CONCLUSION

Pain management in cancer patients is an important and difficult task. In patients for whom anticancer therapy provides no relief or who have recurrence of pain that is not amenable to further palliative measures, it is essential to treat the pain symptomatically. RF ablation provides a potential alternative method for palliation of painful osteolytic metastatic lesions; the procedure is safe, and the pain relief is substantial.

Curative ablation is performed in some specific cases like bone metastases of thyroid cancer. The treatment begins with radio frequency ablation destroying more than 90% of the lesion allowing a radioisotope therapy (¹³¹- iodine) to complete the ablation of residual tumor.

A multidisciplinary approach is essential to determine the course of treatment that best alleviates pain, preserves function, and optimizes the quality of life remaining in the patient with metastatic disease. An combination of different methods could be necessary to treat cancer pain efficaciously and thermal ablation is another modality which could be useful in this therapeutic battery.

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