Tumor-Debulking Void-Enhanced Vertebroplasty

Introduction

Vertebral Compression Fractures (VCFs) are a common ailment afflicting cancer patients with metastases to the spine. Separate from pain directly caused by cancer and associated spinal tumors, VCFs themselves usually cause debilitating back pain resulting in impaired mobility and functionality and reduced quality of life.

Treatment of VCFs secondary to spinal metastases is challenging: surgical fusion techniques are traumatic, leading to long and difficult recoveries; traditional tumor ablation methods do not effectively treat fractures; and standard vertebral augmentation techniques such as vertebroplasty and kyphoplasty have not been widely adopted for this application, mainly due to their increased potential risk for complications.

Vertebral augmentation offers an excellent method for palliating pain and restoring functionality in patients suffering from VCF associated with osteoporosis[1,2]. Recently, both methods have been used to treat VCFs secondary to tumors[3]. Particularly with kyphoplasty, creation of a void in the vertebra allows improved cement injection, which is thought to be associated with lower risk of complications.

Nevertheless, the kyphoplasty approach may be improved even further. Creating a cavity by removing tissue, as opposed to simply displacing it, may have significant advantages over other techniques.

A new technique allows for precise tissue removal from the spine, overcoming the disadvantages of tissue displacement. This method now stands to make vertebral augmentation standard of care for cancer patients with VCFs, by providing potential for pain palliation, improved functionality, and better quality of life during their continued oncologic treatment.

Etiology of the Disease State

Vertebral compression fractures (VCFs) are a common ailment affecting an estimated 750,000 to 1 million patients annually in the USA. Most frequently caused a by deterioration of the vertebral body from osteoporosis, they may also be caused by structural compromise due to a tumor or by excessive compression force induced by trauma.

Tumors or soft tissues lesions are responsible for up to 10% of VCFs. The most common vertebral lesions are secondary cancers that have metastasized from primary sites including the lungs, breast and prostate, among others. Indeed, it is estimated that 50% of patients suffering from lung, breast and prostate cancer will suffer from bone metastasis[4] and the spine is the third most common site in the body for cancer metastases. Infrequently found are primary lesions, which may be benign (including giant cell tumor and hemangioma) or malignant (e.g. multiple myeloma and plasmacytoma). Irrespective of origin, vertebral lesions frequently supplant bone in the vertebral body as they grow, resulting in a loss of structural integrity and ultimate fracture.

The high incidence of spinal metastases and the high risk of resulting VCFs imply that a significant proportion of cancer patients ultimately will suffer from painful VCFs.

The typical patient with this condition has previously been diagnosed with cancer and presents with focal or laterally radiating back pain that is debilitating in nature. Magnetic resonance imaging will usually show the presence of a VCF with lesions evident at the symptomatic level. Current experience suggests that the debilitating nature of the pain results in decreased physical activity and increased morbidity. Left untreated, the patient's health may be expected to decline more rapidly than without fracture.

Historical Treatments

Historically, bed rest and other conservative treatments including the use of analgesics and immobilization have been used to manage patients with VCFs arising from vertebral tumors.

More aggressive treatments have included open spine fusion surgery, conducted with the objective of restoring functionality to the spine. Cancer patients with compression fractures do not respond well to such invasive surgery, as their already high morbidity levels mean that they are not able to cope with the surgical trauma and lengthy recuperation. Indeed it might be expected that a patient with limited life expectancy could spend the balance of their life recovering from their surgery.

The general failure of fusion surgery for cancer patients has led to a changed attitude to the treatment of VCFs — recently the objective has evolved to more palliative treatment options and to the avoidance of traumatic procedures.

Vertebroplasty — Cement Augmentation

The vertebroplasty procedure was introduced in France in 1984, where it was first used to treat patients with VCFs arising from malignant and benign tumors. Vertebroplasty involves the percutaneous insertion of a cannula into the vertebral body (e.g. through the pedicle) and the injection of bone cement (such as poly-methyl methacrylate) to augment the vertebral body. The primary method of action of the procedure is believed to be the stabilization of bone fragments whose movement relative to each other is a cause of significant pain.

Only in the mid-1990s did physicians in the US begin using the procedure predominantly on patients with osteoporosis related fractures. Since then, vertebroplasty has become a standard of care for osteoporotic VCFs, with 85–90% of patients experiencing dramatic or complete pain relief[5]. Furthermore it is a relatively very safe procedure, with a complication rate of approximately 1%[6]. Primary complications involve cement extravazation affecting venous uptake and in rare cases cement penetration of the intervertebral disc space or spinal canal, or embolization into the lungs.

The primary mode of action of the vertebroplasty is believed to be fracture immobilization. Since its inception, vertebroplasty has been used in the treatment of VCFs secondary to vertebral tumors, although much less frequently than in the treatment of osteoporotic fractures. Vertebroplasty works well in the palliation of pain for tumor related VCFs, and so it has gained some acceptance as an effective treatment.

The presence of soft tissue lesions in the vertebral body has significant implications for cement injection, primarily due to the different physical properties of tumor soft tissue and the more fluid marrow, fat and blood that usually occupy the interstices between the vertebral trabeculae.

First, the solid nature of most tumors makes them difficult to displace through vertebral bone, with the result that the cement injection pressure for tumor related VCFs is higher than for osteoporosis-induced fractures. Typical cement injection pressures within the vertebral body are six times higher where soft tissue lesions are involved, measuring 5.8 psi versus 1.0 psi where no lesions are involved[7]. Presumably osteoporotic fractures are even lower.

Second, the high required injection pressure in association with the idiosyncratic geometry and tissue morphology of tumors may be a significant reason for the higher vertebroplasty complication rates for tumor (10%) versus osteoporosis (1.3%) related fractures[8]. It is believed that this is because tissue morphology and geometry make cement flow unpredictable, and the relatively high cement injection pressure gives cement the ability to move very rapidly into new and often undesirable locations when it breaches the barrier offered by the soft tissue lesion.

For these reasons, vertebroplasty is not as widely applied in the treatment of tumor related VCFs as might be expected. In fact recent attempts have been made to overcome the limitations of the vertebroplasty procedure in treating this disease state. Notably, however, all other methods of treatment of tumor related VCFs still involve the augmentation of the vertebral body with cement as with standard vertebroplasty, but vary in their approach to the treatment of the tumor tissue prior to cement injection.

Thermal Tissue Ablation

Thermal tissue ablation involves the insertion of a bipolar radiofrequency (RF) device designed to pass RF energy through tissue to induce thermal necrosis. Devices such as the StarBurst (Rita Medical, Fremont, CA), designed for application in organs such as the liver, have been used in the treatment of vertebral tumors, and have demonstrated effectiveness in killing tumors in the spine.

Notwithstanding the demonstrated effectiveness of these devices in causing necrosis of tumors, there has been no evidence that suggests that this necrosis has an effect to overcome the limitations of cement injection in the vertebroplasty procedure. There is no evidence that the RF tumor ablation sufficiently alters the morphology of the tumor tissue to allow easier or safer injection of cement.

From this perspective it is important to describe the rationale for inducing thermal necrosis of vertebral tumor tissue in the presence of vertebral compression fractures. If the objective is to treat the tumor itself, then thermal ablation is a rational clinical treatment, but this goal may be inappropriate, depending on the patient's disease. For primary malignant lesions in the spine, eradication is paramount. For primary benign lesions, tumor destruction may be useful, but fracture augmentation for palliation of pain will likely be the overriding concern. In the majority of cases, the spinal tumor will be secondary to cancer elsewhere in the body, with the result that treatment of the primary cancer is the principal long-term issue, and palliation of pain to reduce morbidity and restore functionality will be the immediate issue.

Although it is clinically demonstrated that patients with spinal metastases demonstrate a proclivity to subsequent metastases, it is not sufficiently demonstrated that the disease spread within the spine is either due to spread of the existing spinal metastases or due to multiple metastases of the primary cancer.

And so in the majority of cases, there is no clinically based rationale for thermal RF ablation of vertebral tumors. Given that there is no evidence to suggest that tissue is physically removed during thermal RF ablation, and no evidence to suggest that tissue morphology is sufficiently altered to allow for improved cement injection, it is likely that thermal RF ablation does not improve the conditions for cement delivery in any material way.

Consequently, there is no published clinical basis for the proposition that thermal RF ablation will improve control of cement delivery, improve the quantity of cement delivered nor improve the quality of the ultimate augmentation achieved.

Kyphoplasty — Cement Augmentation in Association with Tamponade Void Creation

Void creation using a tamponade device is a means for offering controlled cement injection for VCFs secondary to spinal metastases. This technique, used extensively in treating compression fractures secondary to osteoporosis, involves the insertion of a tamponade (usually a balloon) into the vertebral body and the expansion of the tamponade to displace bone and tissue to create a void. Cement is subsequently injected into the void, completing the procedure. This procedure is commonly referred to as balloon kyphoplasty or balloon-assisted vertebroplasty.

To date, a small number of pilot studies have demonstrated the effectiveness of balloon kyphoplasty in pain palliation for patients with VCFs secondary to metastatic disease. In one specific series of 18 kyphoplasty patients with multiple myeloma who underwent 55 augmentation procedures, significant pain relief was achieved in all patients[9].

The evidence to date supports the use of this procedure in the palliation of pain. Indeed, the results indicate that cancer patients with VCFs benefit from comparable pain palliation of 90–95% as with standard vertebroplasty. As with vertebroplasty, the pain relief is generally attributed to fracture stabilization from the introduction of cement.

In addition to the comparable pain palliation results, it has been suggested that the benefit of injecting cement into the void in the vertebral body is increased control of the cement delivery, with the potential for a reduced risk of complications. Notwithstanding the fact that no studies have demonstrated conclusively that this is the case, it seems plausible that the preparation of a void will allow cement injection at lower initial pressures, and will allow for the predictable placement of cement within the void. From this perspective, kyphoplasty may offer a valuable enhancement to standard vertebroplasty cement augmentation.

Despite the fact that the postulated benefits of using kyphoplasty for metastatic VCFs seem valid, adoption has been very slow, possibly because of two limitations of the procedure:

Metastatic Cell Embolization. The expansion of a tamponade within a metastatic lesion displaces tissue to create a void. This action forces tissue from within the vertebral body to embolize into the blood stream. In osteoporotic bone the tissue displaced includes fat blood and bone marrow whereas in tumor related fractures metastatic cells themselves may be ejected into the blood stream risking further metastasis to other parts of the body.

Risk of Retropulsion. The tissue displacing effects of an expanding tamponade carry an attendant risk of tissue retropulsion with possible neurologic consequences. Indeed in vertebral fracture secondary to metastatic disease this risk can be heightened because a non-fluid tumor mass will tend to be displaced 'en bloc' implying that the force of tamponade expansion may be directly applied to the spinal cord or other neural elements. In cases with posterior cortex disruption or cortical dissolution this tissue migration can be difficult or impossible to observe fluoroscopically.

Despite the clear advantages of kyphoplasty over vertebroplasty, these two factors are significant in evaluating the appropriateness of kyphoplasty as a treatment option for these patients.

An Improved Procedure

Tissue Removal vs. Tissue Displacement

Overcoming the disadvantages of kyphoplasty whilst realizing the benefits of void creation for cement augmentation could offer metastatic VCF patients a significantly better treatment option than any previously available. Recognizing that kyphoplasty's limitations stem from its use of a displacement mechanism to create a void, the most promising means of overcoming these limitations is to create a void by tissue removal instead of tissue displacement.

In light of the foregoing discussion, traditional open surgical approaches for tissue removal have their own disadvantages. Therefore, a device that can remove tissue via the same percutaneous access commonly used for kyphoplasty and vertebroplasty can offer significant advantages. The use of a device to volumetrically remove tissue via focused ablation, in conjunction with cement augmentation, may offer the best treatment option for metastatic VCF patients, without the limitations of previous procedures.

Bipolar Radiofrequency Plasma Ablation

As discussed above, bipolar RF is a technology commonly used for the thermal tissue necrosis, particularly the necrosis of malignant lesions. In the mid-1990s a unique form of bipolar RF was developed to ablate tissue without a thermal effect. This proprietary technology involves the use of saline or Ringer's lactate solution around the bipolar electrode array, and the passage of a distinctive RF current through the fluid to cause ions in solution to energize into a focused ionic plasma cloud[10]. The affect on the target anatomy is that tissue touching the plasma is completely dissolved via a process of molecular dissociation as ions break the intramolecular bonds within cells. Dissociated tissue is turned into elemental gases which typically exit the surgical site.

There are three significant benefits to the use of this plasma-mediated approach to bipolar RF tissue treatment. First, tissue interacting with the plasma is completely dissociated with the result that the tissue is removed instead of merely killed. Second, the plasma cloud is tightly controlled providing the ability for highly targeted tissue removal. Third, the created plasma field is not especially hot, because the energy created is ionic and not thermal in nature. The result is that tissue immediately adjacent to the ablation suffers only minimal thermal damage.

These three factors have led to the wide adoption of bipolar plasma RF technology as a standard of care in procedures where precise tissue removal or minimization of collateral tissue damage, or both, are required. Examples include orthopedic procedures such as shoulder surgery, and ENT procedures such as tonsillectomy.

Due to its distinctive benefits, bipolar plasma RF technology is uniquely suited to debulking tumor tissue prior to cement augmentation. It offers the ability to remove tumor tissue in a highly targeted manner allowing for the creation of a cavity without tissue displacement. Furthermore, it removes tissue with minimal thermal injury at the margin[11].

Procedure Description

The bipolar plasma tumor debulking procedure is relatively straightforward and comprises the following steps:

STEP 1
Patient Preparation

- Patient should be prepared pre-operatively using standard procedures percutaneous spine surgery.
- Introducer cannula should be inserted to access desired treatment area.
- The optimum trajectory should be selected to ablate maximum tissue volume (Illustration 1).
- Standard needle insertion precautions should be followed.

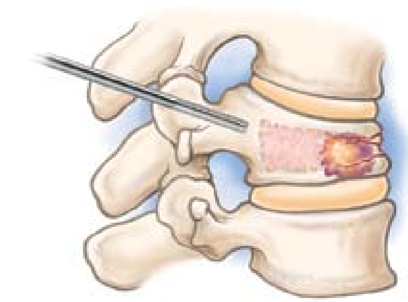

Illustration 1: Standard percutaneous access.

STEP 2
Insert Bipolar Plasma RF Device

- The device should be inserted under careful fluoroscopic monitoring (Illustration 2).
- Saline Flow should be enabled.
- If necessary, after the tip of the device is fully deployed, the device may be activated to facilitate advancement into the target tissue.
- Using fluoroscopic guidance verify that the device is within the target tissue.

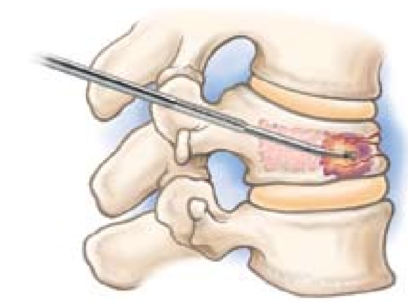

Illustration 2: Ablation device inserted.

STEP 3
Use Bipolar Plasma RF Device to Ablate Tissue and Create a Cavity

- While monitoring the patient carefully, activate the device and advance through the spine to ablate tissue and create a cavity (Illustration 3).
- If necessary, maneuver device back and forth during ablation to break through hard tissue.
- After each pass with the device, withdraw and ablate forward again along another axis. Cease making passes once resistance subsides.
- If neural stimulation is observed, pause ablation, verify positioning and recommence ablation.

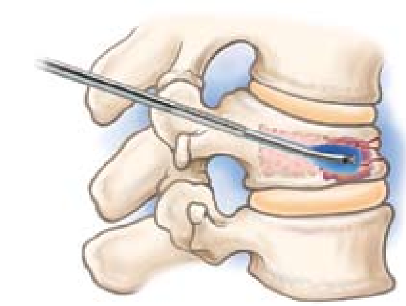

Illustration 3: Debulking soft tissue via ablation.

STEP 4
Inject an Approved Augmentation Material into the Cavity Created in the Spine.

- If desired, use patient positioning to extend the spine and facilitate fracture reduction.
- Using standard injection technique, inject cement into the created cavity in the spine (Illustration 4).
- Use continual fluoroscopy to monitor cement flow.
- Once desired cement penetration is achieved, cease injection and withdraw cannula.
- Follow standard post-operative guidelines.

Note that the injection of a cement is considered a separate procedure.

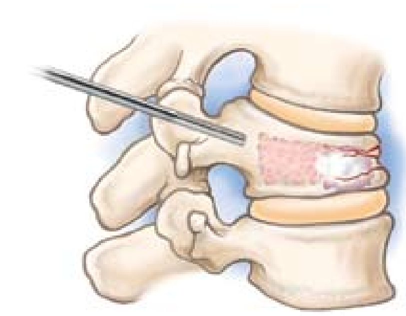

Illustration 4: Cement augmentation.

Initial Clinical Experience

Pre-clinical

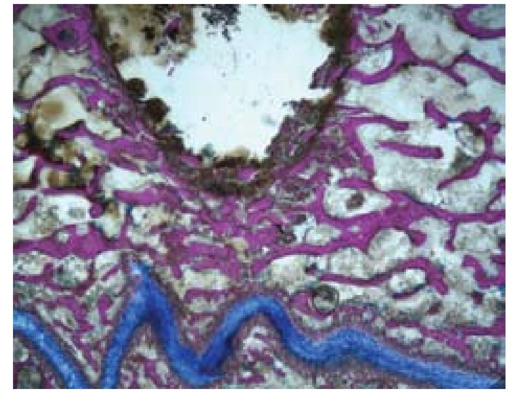

Illustration 5: Histology image post-ablation.

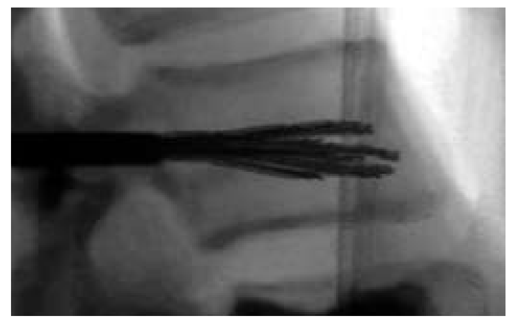

Illustration 6: Registered device images for volume estimate.

Pre-clinical science involving a bipolar RF plasma tissue ablation device has included *in-vivo* work focused on temperature and histologic analysis, and also *ex-vivo* ablation volume analysis.

Initial temperature and histology analysis was performed by ablation tissue in the spine in an *in-vivo* porcine model (Do, H. and Rippy, M. Presented at Congress of Neurological Surgeons, Boston, MA, October 2005). A series of temperature measurements were taken within 2–3mm of the device tip during activation. The maximum recorded temperature was 48° C. Histological analysis of bone (Illustration 5) immediately adjacent to the tissue ablation zone found no evidence of clinically relevant injury.

The volume of tissue removed by a bipolar RF plasma tissue ablation device will vary depending on the size of the access cannula and the configuration of the device itself. In one example of a spinal tissue ablation procedure, radiographic images of a series of device positions were registered and overlaid (Illustration 6), and measurements of the diameter of the conical region occupied by the ablation device were collected. The calculation of the estimated cavity volume ablated was 1.67 cm^3, based on a total ablation length, from the tip of the access cannula, of 33mm.

Intra-Operative Assessment

Intra-operative assessment of the dimensions and location of a vertebral cavity created by a bipolar RF plasma ablation device is easily accomplished. Although a physician can assess the cavity by observing a variety of device positions fluoroscopically, the placement of a conforming device can allow a physician to observe the full scope of a void in a single image. This may be performed by inserting a conforming balloon and inflating with contrast or, more commonly, by deploying a flexible angio guide-wire down the cavity into the void (Illustrations 7 & 8).

Illustration 7

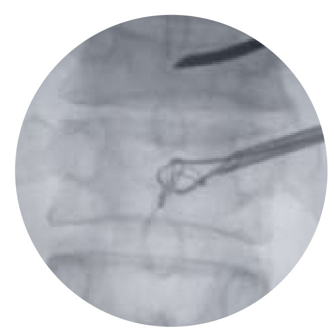

Illustration 8

Images courtesy of Dr. Giovanni Anselmetti, Turin, Italy.

Patient Outcomes

Initial experiences using a bipolar plasma RF tissue ablation device for tumor debulking enhanced vertebroplasty removal have been promising.

A patient series presented at ASSR[12] in 2006 describes results for 36 treated levels in 28 patients with VCFs secondary to spinal lesions. Tissue removal was used debulk the tumor mass to facilitate cement augmentation in all cases. Adequate cement delivery was achieved in all cases, with 2/36 (6%) instances of cement extravasation outside the presumed vertebral boundaries. Both instances of extravasation were clinically inconsequential. All patients experienced marked pain palliation.

Case Example

In this case, a 76 year-old man presented with severe focal and radiating low back pain. MRI (Illustration 9) and CT (Illustration 10) analysis highlighted metastatic lesions with associated VCFs of the L1 and L3 vertebrae. Biopsy results indicated metastasis from previously undiagnosed hepotoma confirmed by subsequent MRI.

Illustration 9: Pre-operative saggital CT of L1-L3.

Illustration 10: Pre-operative saggital MRI of L1-L3.

The lesion in the L1 vertebra (Illustration 11) was located centrally in the posterior of the vertebral body with associated disruption of the posterior cortex. Bilateral cavity creation with a bipolar plasma ablation device was targeted at partial debulking of the lesion and removal of vertebral tissue anterior to the lesion to limit the risk of tissue retropulsion and to allow for safer cement injection.

The L3 vertebra involved a lesion to the anterior (Illustration 12) of the vertebral body with associates cortical disruption. Bilateral ablation into the lesion was performed in this instance with the goal of providing support to the unstable anterior of the body.

Illustration 11: Pre-operative axial CT of L1.

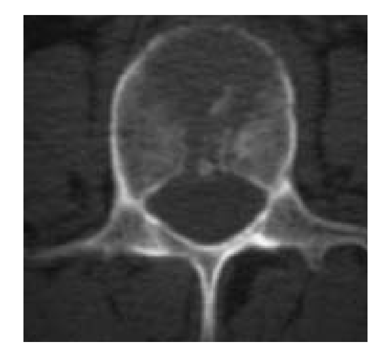

Illustration 12: Pre-operative axial CT of L3.

In both levels, cement was delivered slowly using a hand-cranked delivery system for optimal control. Delivery was performed under live fluoroscopy through the bilateral cavities, and interdigitated beyond into the trebeculae (Illustrations 13, 14, 15, 16 & 17) to immobilize the fracture and strengthen the vertebrae. In both levels, cement was contained within the presumed vertebral boundaries apart from a small clinically insignificant extravasation at the anterior of L3 (Illustration 15).

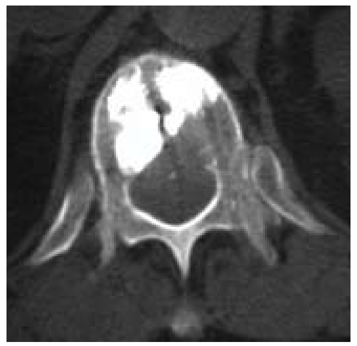

Illustration 13: Post-operative axial CT of L1.

Illustration 14: Post-operative axial CT of L3.

Illustration 15: Post-operative lateral fluoro image of L1.

Illustration 16: Post-operative lateral fluoro image of L3.

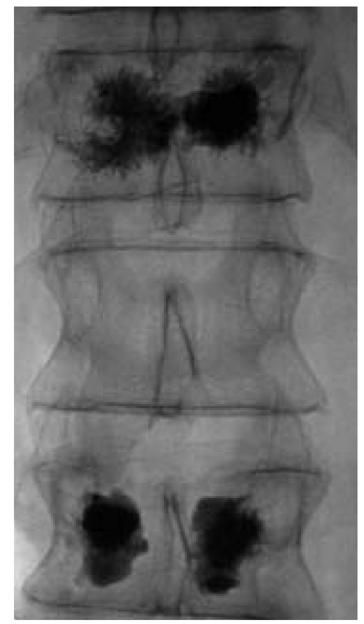

Illustration 17: Post-operative AP fluoro image of L1-L3.

Case and images provided by Bassem Georgy MD, San Diego, CA.

The patient was admitted and monitored overnight. Fracture related pain was significantly diminished within two days of the procedure. The patient was able to substantially resume normal life activities and continue with oncologic treatments.

Conclusion

The presence of soft tissue arising from metastasis to the vertebral body represents a significant challenge to the treatment of vertebral compression fractures. Vertebral augmentation procedures, which offer the best option for pain palliation and improved functionality for VCF sufferers, have been limited in their application due to inherent difficulties posed by the presence of soft tissue. The creation of a void in the vertebral body offers significant advantages over direct cement injection, improving the viability of the procedure. Furthermore, the creation of a cavity via tissue removal offers distinct advantages over void creation via displacement.

Augmentation of VCFs has the potential to improve functionality and mobility, reduce pain and improve quality of life in cancer patients. It also may be performed without compromising the effectiveness of continued oncologic treatments.

The use of bipolar plasma RF technology represents a significant leap forward in tissue ablation in the spine, offering new treatment options to patients who traditionally have had limited treatment options available to them. Detailed clinical study is needed and is currently underway to demonstrate the effectiveness of this promising new application.

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