The invention relates to methods for treating diseased bone, particularly bone that is afflicted with cancer. More specifically, the present invention relates to methods for treating diseased bone using localized anti-cancer therapy.
Treatment of Vertebral Cancer with $^{153}$Samarium

Cross Reference to Related Applications

This application claims benefit from U.S. Provisional Application Ser No 60/924,871, filed June 4, 2007, which application is incorporated herein by reference.

Field of the Invention

The invention relates to methods for treating vertebral cancers using localized administration of anti-cancer agents.

Background of the Invention

Vertebroplasty and kyphoplasty are minimally invasive percutaneous techniques that revolutionized the treatment of painful vertebral body compression fractures due to osteoporosis and bone metastases. These procedures initially developed in France over 10 years ago, and are now routinely used in the U.S. Kyphoplasty involves extra- or transpedicular cannulation of the vertebral body under fluoroscopic guidance, followed by insertion of an inflatable bone tamp. Once inflated, the tamp may restore the vertebral body toward its original height, while creating a cavity to be filled with bone cement. Cement is injected under a relatively low and safe pressure, thus preventing extra-vertebral leakage.

Kyphoplasty is an effective procedure to alleviate pain in metastatic vertebrae.

$^{153}\text{Samarium-EDTMP}$ (Quadramet®) is used for palliative treatment of multiple bone metastases. The hematological toxicity is the main limiting factor. $^{153}\text{Samarium}$ is a targeted radio-pharmaceutical, with a half-life of 46.3 hours, currently approved by the U.S. Food and Drug Administration (FDA) to relieve bone pain in patients who have confirmed metastatic bone lesions that are evident on a bone scan. Quadramet, a samarium carrying agent, is used to treat pain associated with prostate, breast, and other cancers that have metastasized to the bone. Unlike opiates and other analgesics, Quadramet offers a systemic yet highly targeted non-narcotic method for treating bone pain, thereby avoiding potential side effects associated with other forms of treatment.

In addition to $^{153}\text{Samarium}$, Quadramet contains the bone-seeking agent ethylenediamine-tetra-methylene-phosphonic acid (EDTMP), which is designed to target areas where cancer is attacking bone. This targeting means that healthy bone and other normal tissues receive much lower exposure to radioactivity. Quadramet ($^{153}\text{Sm EDTMP}$) has an affinity for bone and concentrates in areas of bone turnover. In clinical studies employing planar imaging techniques, more Quadramet accumulates in osteoblastic, osteolytic lesions than in normal bone with a lesion-to-normal bone ratio of approximately five. The mechanism of action of Quadramet in relieving the pain of bone metastases (e.g., vertebral mets) is not fully understood.
established It is hypothesized that the radioactive samarium concentrating in the vertebral site, disrupts the malignant process in such a way that it leads to pain relief.

Human protein binding has not been studied, however, in dog, rat and bovine studies, less than 0.5% of $^{153}$Sm-EDTMP is bound to protein. At physiologic pH, >90% of the complex is present as $^{153}$Sm [EDTMP]-5, and <10% as $^{153}$SmH [EDTMP]-4. The octanol water partition coefficient is <10$^5$.

The greater the number of metastatic lesions, the more skeletal uptake of $^{153}$Sm radioactivity. The relationship between skeletal uptake and the size of the metastatic lesions has not been studied. The total skeletal uptake of radioactivity was 65.5% ± 15.5% of the injected dose in 453 patients with metastatic lesions from a variety of primary malignancies. In a study of 22 patients with a wide range in the number of metastatic sites, the percentage of the injected dose (% ID) taken up by bone ranged from 56.3% in a patient with 5 metastatic lesions to 76.7% in a patient with 52 metastatic lesions.

The complex formed by samarium and EDTMP is excreted as an intact, single species that consists of one atom of the $^{153}$Sm and one molecule of the EDTMP, as shown by analysis of urine samples from five patients who were administered samarium ($^{153}$Sm-EDTMP). Metabolic products of samarium ($^{153}$Sm-EDTMP) were not detected in humans.

For Quadramet, calculations of the % ID detected in the whole body, urine and blood were corrected for radionuclide decay. The clearance of activity through the urine is expressed as the cumulated activity excreted. The whole body retention is the simple difference between the injected dose and the cumulated urine activity excreted.

Clearance of radioactivity from the blood demonstrated biexponential kinetics after intravenous injection in 19 patients (10 men, 9 women) with a variety of primary cancers that metastasized to the bone. Over the first 30 minutes, the radioactivity (mean ± SD) in the blood is decreased to (15 ± 8)% of the injected dose with a half-life ($T_{1/2}$) of (5.5 mm ± 1.1 mm).

After 30 minutes, the radioactivity cleared from the blood more slowly with a $T_{1/2}$ of (65.4 mm ± 9.6 mm). Less than 1% of the injected dose remained in the blood for five hours after injection.

Samarium $^{153}$Sm-EDTMP radioactivity was excreted in the urine after intravenous injection. During the first 6 hours, (34.5 ± 15.5%) were excreted. Overall, the greater the number of metastatic lesions, the less radioactivity was excreted.

In a randomized clinical trial comparing Quadramet to placebo, there was evidence of doubling of hematological adverse events. Out of those who were randomized to the quadramet arm, 41% had decreased hemoglobin and 59% had leucopenia compared to 23% and 7% respectively in the control arm.
Quadramet is approved for bone metastases as 1 mCi/Kg body weight intravenous injection. The following table demonstrates the absorption by bone surfaces and bone marrow in 70 kg body weight patients.

<table>
<thead>
<tr>
<th>Target Organ</th>
<th>Rad/mCi</th>
<th>mGy/MBq</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone Surfaces</td>
<td>25 0</td>
<td>6.76</td>
</tr>
<tr>
<td>Red Marrow</td>
<td>57 0</td>
<td>1.54</td>
</tr>
</tbody>
</table>

Administration of radioactive substance (Liquid or solid) in a cavity or tissues containing neoplasm is a well established technology where a radioactive material such as $^{198}$Au, $^{32}$P, etc. is injected or implanted strictly in the malignant tissue with the objective of extinguishing the malignancy and alleviating symptoms.

An object of the present invention is to provide localized administration of an anti-cancer agent to subjects suffering from painful vertebral metastases in order to achieve the immediate benefit of the agent without the attendant consequences.

**Summary of the Invention**

The invention generally provides a method for treating metastases of the vertebral column in a subject's body. The method includes creating an internal space or lumen within a vertebral body of the subject and disposing an anti-cancer agent within the created internal space.

In another embodiment of the invention, a method for delivering radioactive emissions to an internal space or lumen in a resected vertebral body is provided.

In other aspects of the present invention, a method for treating vertebral metastases is provided. The method includes the steps of surgically resecting a vertebral body to create an internal space or lumen, placing an expandable member within the lumen in order to expand the internal space or lumen, delivering a composition comprising an anti-cancer agent to the expanded space, and sealing the lumen.

In certain embodiments of the invention, the anti-cancer agent is a radiation source that is disposed within the lumen of a vertebral body.

Another embodiment of the invention provides a method of treating vertebral cancer, which includes identifying the vertebral cancel site on the surface of the vertebral column, forming a lumen at the site through an access site on the vertebral column, inserting a composition comprising a filler and a therapeutically effective amount of an anti-cancer agent into the lumen, and sealing the lumen.
Detailed Description

For the purposes of the invention described in this application, the certain terms shall be interpreted as shown below.

The term ‘cannula’ as used herein describes a slender hollow tube or pipe of circular cross-section, used in medical procedures, wherein it is designed to be insertable into a body cavity, duct or vessel. During the insertion of the cannula, the lumen (interior) is often occupied by a trocar as a stiffening means. In orthopedic procedures such a device is commonly referred to as a bone needle.

The term “trocar” as used herein describes a surgical tool, instrument or device used to puncture and cut through body tissue comprised of a sharply pointed solid or hollow shaft, wherein the point can have any functional geometry such as conical, pyramidal, blade-like, drill-like, etc. A trocar is often deployed within a cannula and functions as a portal for the subsequent placement of other devices. It is also commonly referred to in medical literature as a stylet.

The term "osteotome" as used herein describes any of the various surgical devices such as a curette or drill that is used to cut, shape, displace, remove, distract or create a void in osseous (bones) tissue.

The present invention generally provides a method for treatment of vertebral metastases, *i.e.*, vertebral cancer, by delivering an anti-cancer agent to tissue and/or bone surrounding an internal space or lumen. Although the method can be used for a variety of purposes, it is preferably used to treat vertebral metastases

In general, the method first includes identifying the site of vertebral cancer on the surface of the vertebral column of a subject. The identification of the cancer can be carried by using a combination of imaging techniques and biopsy sampling. A cannula (small tube) is advanced down the subject’s vertebral column and a sample of bone is collected and sent to pathology as a biopsy specimen. After the site of the cancer has been identified, the mass of cells constituting the cancer is removed. The cancer may be excised using a curette to remove tissue by scraping or scooping. The removal of the cancer creates a lumen or internal space within the vertebral column. Following the formation of a lumen, a composition comprising a filler and a therapeutically effective amount of an anti-cancer agent is inserted into the lumen. Imaging techniques such as fluoroscopy may be used to monitor for any possible extrusion of the cement beyond the anatomic boundary of the vertebral body. After the insertion of the composition, the lumen is sealed by appropriate methods such as using bone cement or a membrane seal.

The method of the present invention is adapted to control the distribution of the anti-cancer agent to tissue surrounding the internal space or lumen. One advantage to controlling the distribution of the agent such as radiation to tissue surrounding the internal space is that a
minimum prescribed dose can be delivered to the tissue in the target treatment region without over-exposing radiation-sensitive tissue, which can cause healthy tissue necrosis.

In one embodiment, the anti-cancer agent is a radiation source. A preferred radiation source that is suitable in the methods described herein is $^{153}$Samarium. This isotope is an ideal choice for the methods of treatment claimed herein, because of its previously known efficacy in the treatment of prostate, breast and other cancers that have metastasized to the bone.

In an embodiment of the invention, the radiation source comprises a radioactive substance such as $^{153}$Sm-EDTMP. This substance has an affinity for bone and concentrates in areas of bone turnover, and particularly targets areas where the bone is attacked by cancer.

In certain embodiments of the invention, the internal space or lumen is formed in the vertebral column through the use of a drilling step using a drill.

The lumen or internal space that is created upon excision of the cancer may be of any shape. Preferably, the shape of the lumen is either linear or curved.

An aspect of the invention provides a method for treating vertebral cancer in a subject by identifying the vertebral cancer site on the surface of the vertebral column, forming a lumen at the site through an access site on the vertebral column, inserting a composition comprising a filler and a therapeutically effective amount of an anti-cancer agent into the lumen, and sealing the lumen.

In certain embodiments of the invention, the filler that is used is bone cement. In other embodiments of the invention, a thermoplastic and transparent plastic such as polymethylmethacrylate (PMMA) may be used to fill the lumen space that is created by virtue of excision of the cancer cells.

In an embodiment of the invention, a cancer is first excised from a location on a subject's vertebral column. Following this step, a size-expansion device is inserted into the cavity or lumen formed as a result of the excision of the cancer. The size-expansion device expands the size of the lumen (as is known from kyphoplasty procedures). Following the expansion of the lumen, a first amount of filler is administered into the lumen. This first amount of filler is sometimes referred to as "head cement" and demarcates a portion of the lumen from the surrounding tissue. The composition comprising the anti-cancer agent is inserted after the first amount of filler. The insertion of the composition is followed by the administration of a second amount of filler, which is sometimes known as "foot cement." The lumen is then sealed by appropriate methods such as using bone cement or a membrane seal.

Methods of the invention can suitably employ size-expansion devices that are selected from the group consisting of a mechanical tamp, a reamer, a drill, a hole puncher and a balloon catheter. Where the size-expansion device is a balloon catheter, it comprises a tube having a distal end and a proximal end, and an expandable structure.
In an embodiment of the invention, the vertebral column is accessed at a particular location and the lumen or internal space is created at that location. In such an instance, the access site and the site of treatment, i.e., where the composition containing the anti-cancer agent is inserted, are present at the same location. In other embodiments of the invention, the access site may be located away from the site of treatment. In this case, the lumen is formed at the access site and extends to the treatment site. After formation of the lumen, the composition containing the anti-cancer agent is inserted into the lumen at a location that is proximate to the site of treatment.

The access site in the methods of the invention may be located in the thoracic, sacrum and lumbar regions of the vertebral column. In certain cases, the access site may be located at a healthy portion of the vertebral column.

A method according to the invention for treating vertebral metastases and other malignancies begins by surgically resecting a vertebral body to create an internal space or lumen. Following tumor resection, but prior to closing the surgical site, the surgeon intravertebrally places a radiation source within the internal space for delivering a controlled dose of radiation to the tissue surrounding the internal space.

An embodiment of the invention provides a method for treating vertebral cancer in which a lumen is formed from the anterior surface of the sacrum, and extends through the sacrum, and through at least one disk and into at least one vertebrae. A composition comprising a therapeutically effective amount of $^{90}$Sm-EDTMP is inserted into the lumen thus formed.

A person having ordinary skill in the art will appreciate that the methods of the present invention can have virtually any configuration, and the embodiments illustrated and described herein are intended merely as exemplary embodiments and should not be construed to limit the present invention. Moreover, it will be understood that the foregoing is only illustrative of the principles of the invention, and that various modifications can be made by those skilled in the art without departing from the scope and spirit of the invention. All references cited herein are expressly incorporated by reference in their entirety.

**Working Example**

The purpose of the experimental methods is to determine the effect of mtravertebral injection of radioactive Samarium during kyphoplasty on the relief of pam resulting from vertebral metastases. It is also desired to evaluate the effect of this procedure on the size of the vertebral metastatic deposits as measured radiographically (CT and MRI).

To determine the effect of this procedure on the quality of life measures for the patients treated by this protocol.
Without further description, it is believed that one of ordinary skill in the art can, using the preceding description and the following illustrative examples, make and utilize the agents of the present invention and practice the claimed methods. The following working examples describe embodiments of the present invention and are not to be construed as limiting in any way the remainder of the disclosure.

**Methods**

IRB approval for an off label use of $^{15}$Sm-EDTMP was obtained. Six patients with documented vertebral bone metastasis and pathological compression fractures were studied (Thoracic in 2 and lumbar m 4). Primary cancel was in lung (2), prostate (1), maxillary sinus (1), myeloma (1) and colon (1). Serial dilution of $^{153}$Sm was performed to obtain 2 mCi/ml. Kyphoplasty procedure was carried out using the known protocol. 2 mCi of $^{153}$Sm was admixed with the bone cement and administered under tight radiation safety measures. Serial nuclear body scans were obtained. Pam assessment was evaluated using analog pam score at 1, 7 and 30 days. Serial blood counts are followed.

**Patient Selection and Inclusion Criteria**

1. The patient must be 18 years of age or older.
2. The patient must have histologically proven malignancy at a primary site (e.g., breast, prostate, or lung).
3. The patient must have a radiographic evidence of bone metastasis, and this must have been performed within 8 weeks prior to enrollment in the study. Acceptable studies include plain radiographs, radionuclide bone scans, computed tomography scans, magnetic resonance imaging, and PET-CT scan.
4. The patient must have an intact anterior wall of the spinal canal.
5. The patient must have significant pam (score 6 or above), which appears to be related to the radiographically documented metastatic vertebra (e) in concern, as measured by the attached "Visual Analog Scale".
6. The patient must be surgically and medically accepted for vertebroplasty kyphoplasty.
7. Good performance status (KPS ≥ 50).
8. Expected life expectancy of 6 months or greater, as estimated by the physician in charge.
9. Signed study-specific informed consent prior to enrollment.

**Exclusion Criteria**

1. Epidural soft tissue component.
2 Patients with vertebral metastases and with clinical or radiographic evidence of spinal cord or cauda equina impingement (effacement) or compression
3 Inability to undergo anesthesia
4 Hematologic primary malignancies
5 Patients receiving systemic radiotherapy (90Sr or 125Sm) within 30 days prior to enrollment

Pretreatment Evaluation
1 History and physical and Karnofsky performance status
2 Radiographic report documenting bone metastases within eight weeks prior to enrollment
3 Neurological examination by the neurosurgeon
4 Pam assessment score measured by the “Visual Analog Scale”
5 Negative pregnancy test for females of childbearing potential within seven days prior to enrollment
6 Physician prediction of patient survival
7 Completion of the pam and quality of life questionnaires

Registration Procedures
The Institutional Review Board (IRB) approval and reapproval must be obtained prior to accession of cases. Patients who meet the eligibility criteria in the Eligibility Check and Section 30, sign the informed consent form, and pass the pretreatment evaluation in Section 40, will be enrolled into the study. The Research Associate at the Radiation Oncology department must be involved in each of these steps to assure high quality data and timely follow-up assessments.

Study Procedures
Protocol
1 Patients with bone metastases are identified at a weekly meeting
2 If the patient is eligible to this study, the protocol will be offered to him/her. If the patient accepts, informed consent will be obtained
3 The case will be scheduled jointly by Neurosurgeon and Radiation Oncologist
4 Radiation physicist orders the radioactive samarium

During the procedure
1 Neurosurgical procedure (kyphoplasty vertebroplasty) is performed as standard using mild general sedation and local anesthesia
2 Once a cavity is identified in fluoroscopy, the trocar is secured. The volume and pressure of the kyphoplasty balloon are recorded.

3 According to standard practice, only the radiation team (Radiation oncologist, Physicist) is handling the radioactive material. All work is done under sterile conditions.

4 Two mCi of Samarium is prepared after serial dilution steps under radiation precautions in the department of radiation oncology and material is transferred to OR.

5 0.5 ml of "Head Cement" is administered first to act as a seal.

6 The Samarium is then introduced into the vertebral cavity using a 2-way valve by the Radiation Oncologist. Total of 0.5 ml (Samarium+O 2 ml radio opaque material).

7 The "Foot cement" (0.5 ml) is then introduced via the same 2-way valve into the vertebral cavity by the neurosurgeon to flush any remains of radioactivity in the system.

8 The two-way valve is then removed and the rest of kyphoplasty/vertebroplasty is ensuied as per their ordinary protocol.

9 Final volume of cement injected is recorded.

10 After securing the wound, all devices, syringes, gloves and basms used for handling the radioactive substance are collected in a "red bag" and stored by radiation safety officer in the hot lab until full radioactive decay.

11 The room is scanned after patient's discharge, any spillage should be reported to radiation safety officer and normal procedures for environmental protection are ensuied.

Post Procedure

1 Normal neurosurgical recovery room protocol is employed. No radiation precautions needed.

2 Patient can be discharged home. No delays because of radiation precautions.

3 Once patient is cleared, a nuclear imaging scan is obtained with Gamma camera. The ratio of uptake in the vertebra to background is calculated. Moreover, Full body scan is obtained to identify other areas of uptake if any.

4 A second nuclear imaging scan is done on the 4th day of the procedure (Two half lives) to document significant decay and calculate dose.

5 MRI/CT scan of the area treated should be done in 4 weeks to assess outcome.

6 Clinical follow up is obtained at 2 & 4 weeks, and in 3 months. Careful pam score assessment is included in each time (Use Study Flow Sheet).
**Drug Therapy**

Quadramet is an FDA approved radioactive injectable substance for patients with bone metastases. Recorded benefits

5 International clinical studies demonstrated that Quadramet is an effective treatment for cancer bone pain in patients with prostate, breast and other cancers. The overall response rate is 70 to 75 percent with approximately half of these responders having marked or complete relief of their pain. There is also less need for external radiation therapy to other areas in the skeletal system.

10 **Side Effects**

The most adverse effect reported due to Quadramet is haematological. A predictable level of dose-related bone marrow suppression was associated with Quadramet treatment. Platelet and white blood cell counts reach low points at weeks three or four with both doses (0.5 to 1.0 mcg/kg) and recovered to normal levels by the fifth week. Even at their lowest, counts were generally higher than those commonly associated with serious complications. Bone marrow toxicity was no greater in women than men despite the fact women tended to enter the published studies with lower platelet and white blood cell counts due to prior marrow-suppressive treatment.

20 **Surgery**

The surgery consists of percutaneous curettage of spinal metastasis, followed by the creation of a void in the vertebral body (kyphoplasty) and injection of bone cement mixed with radioactive material (Samarium) for tumor eradication. This percutaneous vertebral procedure is performed under local anesthesia and intravenous conscious sedation, thus allowing constant monitoring of neurological function of the neighboring nerve roots and spinal cord. The patient is placed in the lateral decubitus position (mostly left), with knees partially bent and the upper arm supported comfortably on an above the head arm rest. The hip is taped to the fluoroscopic table. Biplane fluoroscopy is used throughout the procedure. All procedures are performed unilaterally. A combination of short-acting barbiturates, opiates, and sedative hypnotic agents (primarily propofol) is used when the trocar and drill penetrate the periosteum and cortical bone, in order to avoid patient discomfort. Prior to insertion of the trocar, the needle tract is infiltrated with 10-20 ml of a half-and-half combination of 1% xylocaine and 0.25% marcaine. The use of either a transpedicular or extra-pedicular approach depends on the location of the metastasis in the vertebral body. Once the drill reaches the center of the metastasis, as projected in the fluoroscopic images from the MI pictures, the rotator Kyphon curette is used under continuous real-time fluoroscopic monitoring to curettage as much tumor as possible. Care is taken to prevent perforation of the cortical...
surfaces of the vertebral body. The curette is then removed from the guiding cannula, and suction is applied to its hub to aspirate the dislodged tumor.

A kyphoplasty is then performed through the same cannula used for the curette. The void created in the tumor by the curettage of tissue is then enlarged by inflating a Kyphon inflatable bone tamp (manufactured by Kyphon* as Xpander™ Inflatable Bone Tamp). The bone tamp is inflated by small increments of volume until the bone tamp reaches the vicinity of the vertebral cortex either lateral, posterior, or anterior. Marked irregularity in the shape of the balloon, possibly due to extrinsic compression by bony speckles, and tamp pressure greater than 200 PSI are also indication to stop balloon inflation.

Other Therapy

Physical therapy may be utilized if seen beneficial. Neurosurgery team will advise patients on its timing.

Pathology

Prior to enrollment in the study, a copy of the surgical pathology report must be submitted to the Research office and kept in the patient's research file to document the histological nature of the primary cancer.

Patient Assessments

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Pretreatment</th>
<th>During 1st Week</th>
<th>Follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>History &amp; Physical</td>
<td>x</td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>Histologic Confirmation</td>
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<td>Physician Prediction of Survival</td>
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<tr>
<td>Pregnancy test <em>(as applicable)</em></td>
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<tr>
<td>KPS</td>
<td>x</td>
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<tr>
<td>Pain Score</td>
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<tr>
<td>Nuclear Imaging</td>
<td>x</td>
<td>x</td>
<td>x¹</td>
</tr>
<tr>
<td>Radiographic Assessment²</td>
<td>x</td>
<td></td>
<td>x²</td>
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<tr>
<td>Quality of life questionnaires</td>
<td>x</td>
<td></td>
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</tr>
<tr>
<td>Other Medications</td>
<td>x</td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>CBC/platelet/differential</td>
<td>x</td>
<td>x</td>
<td>x⁴</td>
</tr>
<tr>
<td>Toxicity Measurement</td>
<td>x</td>
<td></td>
<td>x</td>
</tr>
</tbody>
</table>

1 Nuclear imaging scan will be done on the 1st day and on the 4th day after the procedure using the Gamma camera.
2 Follow up schedule will be on the 2 weeks, 4 weeks, and 3 months after the operation.
3 MRI or CT scans will be done at 1 and 3 months.
4 Can be requested after 3 months if clinically indicated.
5 Radiographic assessment *(MRLCT)* must be consistent throughout the study.
Data Collection
1. Case Report forms for each visit will be designed. Data will be collected in a spreadsheet (excel).
2. Once the patient is enrolled in the study, a follow up schedule will be sent to the investigators m charge, and will be kept in the patient's chart.
3. A weekly follow up schedule for the patients on the study with the appropriate case report forms will be given to the investigators to ensure timely follow up.
4. Case report forms and various source documents will be given to the radiation therapy research associate to be kept in the patient's research file.

Statistical Considerations
The primary end point of this study is the frequency and duration of pain relief as determined by the reduction in pain score. The secondary end points include:
1. Feasibility and tolerance to the procedure
2. Patient assessed quality of life
3. Ambulation and preservation of sphincter functions
4. Overall survival from time of enrollment
5. The frequency of severe (> grade 3) toxicities

From our previous observation, it is expected that the pain score will change from at least 0.6 to be 0.2, so setting the \( \alpha \) (statistical level of significance for a two sided test) = 0.05, and the power to be 80%, a sample size of 30 patients will be enough to get a significant conclusion.

Results
All patients tolerated the procedure well. No immediate procedure(s) related morbidities were noted. One case was not technically satisfactory and no significant uptake was detected in the injected vertebra. Nuclear scan done on 0 revealed excellent radiotracer uptake in the other 5 vertebrae injected. The absorbed radiotracer was seen to target other skeletal metastatic lesions in 2 patients. There was no significant change in WBC, HCT or Platelets seen in blood counts obtained over one month post-procedure. Except for the first patient, no appreciable radiation leakage was encountered. Pain score was reduced from a mean of 8.5 to 3.2 during the first week and was maintained below score of 4 at one month assessment.

The combination of intervertebral administration of \(^{154}\)Sm and Kyphoplasty is well tolerated by clinical subjects. No haematological side effects were encountered, probably due to the use of only 2 mCi compared to over 70 mCi in intravenous administration. Pain control was satisfactory at areas treated.

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While the invention has been described and illustrated herein by references to various specific materials, procedures and examples, it is understood that the invention is not restricted to the particular combinations of material and procedures selected for that purpose. Numerous variations of such details can be implied as will be appreciated by those skilled in the art. It is intended that the specification and examples be considered as exemplary, only, with the true scope and spirit of the invention being indicated by the following claims. All references, patents and patent applications referred to in this application are herein incorporated by reference in their entirety.
What is claimed:
1. A method of treating vertebral cancer in a subject in need thereof, comprising:
   a. identifying the vertebral cancer site on the surface of the vertebral column;
   b. forming a lumen at the site through an access site on the vertebral column;
   c. inserting a composition comprising a filler and a therapeutically effective amount
      of a anti-cancer agent into the lumen such that the composition is proximate to a treatment
      site, and
   d. sealing the lumen.
2. A method of treating vertebral cancer according to claim 1, wherein the forming step
   comprises drilling.
3. A method of treating vertebral cancer according to claim 1, wherein the lumen is linear.
4. A method of treating vertebral cancer according to claim 1, wherein the lumen is curved.
5. A method of treating vertebral cancer according to claim 1, wherein the anti-cancer agent
   comprises a radioactive substance.
6. A method of treating vertebral cancer according to claim 5, wherein the radioactive
   substance is $^{153}$Samarium-EDTMP.
7. A method of treating vertebral cancer according to claim 1, wherein the treatment site is
   spaced apart from the access site.
8. A method of treating vertebral cancer according to claim 1, wherein the access site is on a
   thoracic region of the vertebral column.
9. A method of treating vertebral cancer according to claim 1, wherein the access site is on a
   sacrum region of the vertebral column.
10. A method of treating vertebral cancer according to claim 1, wherein the access site is on a
    lumbar region of the vertebral column.
11. A method of treating vertebral cancer according to claim 1, wherein the access site is on a
    healthy region of the vertebral column.
12. A method of treating vertebral cancer in a subject in need thereof comprising forming a
    lumen from the anterior surface of the sacrum through the sacrum, through a disk and into at
    least one vertebrae; and introducing a composition comprising a therapeutically effective
    amount of $^{153}$Samarium-EDTMP into the lumen.
13. A method for treating a vertebral cancer comprising the steps of: excising the cancer from
    a vertebral body to form an internal space or lumen, inserting a size-expansion device into the
    formed lumen, expanding the size of the lumen and filling at least a portion of the lumen with
    a filler.
14. The method of claim 13 wherein the size-expansion device is selected from the group
    consisting of a mechanical tamp, a reamer, a drill, a hole puncher and a balloon catheter.
15. The method of claim 13 wherein the size-expansion device is a balloon catheter comprising: a tube comprising a distal end and a proximal end; and an expandable structure.
16. The method of claim 13 wherein the filler is polymethylmethacrylate.
17. The method of claim 13 wherein the filler is bone cement.
INTERNATIONAL SEARCH REPORT

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 08/65748

A CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61K 51/00 (2008.04)
USPC - 424/1.11

According to International Patent Classification (IPC) or to both national classification and IPC

B FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

USPC 424/1 11

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

WEST (PGPB,USPT,USOCEPAB,JPAB)

Google (Patents, Scholar, and Web)

Search Terms Used cancer vertebral Samarium polymethylmethacrylate lumen

C DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No</th>
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<td>X</td>
<td>US 2007/0055382 A1 (OSORIO et al) 8 March 2007 (08 03 2007), Abstract, para [001], [021], [0028], [0077], [0078], [0087], [0094], [0100], [011]</td>
<td>1-4, 7-11, 13-17</td>
</tr>
</tbody>
</table>

D Further documents are listed in the continuation of Box C

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Mail Stop PCT, Attn ISA/US, Commissioner for Patents
P O Box 1450, Alexandria, Virginia 22313-1450
Facsimile No 571-273-3201

Authorized officer
Lee W Young
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