### STUDY SUMMARY

<table>
<thead>
<tr>
<th>Title</th>
<th>Combining Intraoperative Radiotherapy with Kyphoplasty for Treatment of Spinal Metastases</th>
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</thead>
<tbody>
<tr>
<td>Short Title</td>
<td>Kypho-IORT</td>
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<tr>
<td>Protocol Number</td>
<td>N/A</td>
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<tr>
<td>Phase</td>
<td>Phase I</td>
</tr>
<tr>
<td>Methodology</td>
<td>Prospective, Non-Randomized</td>
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<tr>
<td>Study Duration</td>
<td>24 months</td>
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<td>Study Center(s)</td>
<td>Single Institution</td>
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<td>Objectives</td>
<td>Primary objective: Tolerability/side effects of the IORT (wound healing, infections, bone necrosis, nerve and spinal cord damage, pathological fracture)</td>
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<td>Secondary endpoint: Effectiveness (pain relief, quality of life, narcotic use, tumor response)</td>
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<tr>
<td>Number of Subjects</td>
<td>10 patients</td>
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</table>
| Main Inclusion Criteria| Metastatic patients from solid tumors  
Estimated life expectancy of at least 3 months  
Spinal metastases documented histologically or by imaging  
Age ≥ 50 years  
Karnofsky Index ≥ 70%  
Numeric Pain Intensity Score ≥ 3  
10% or more loss of vertebrae height  
Maximum tumor diameter: 3cm |
| Main Exclusion Criteria| Any pre-menopausal female  
Previous external beam radiotherapy to the potential treatment site  
No systemic radioisotopes within 30 days of procedure |
| Study Procedure        | Intrabeam® Intraoperative Radiotherapy with spinal applicators                           |
| Duration of administration | Intraoperative                             |
| Reference therapy      | Vertebroplasty, Kyphoplasty, External Beam Radiotherapy                                   |
| Statistical Methodology | Wilcoxon signed rank tests and Mann-Whitney Rank Sum                                      |
ELIGIBILITY CHECKLIST:

____(Y)  1. Is there histologic confirmation of a primary tumor origin?

____(Y)  2. In the estimation of the investigator, does the patient have a life expectancy ≥ 3 months?

____(Y)  3. Has the patient completed the "Numeric Pain Intensity Scale" questionnaire?

____(Y)  4. Is there radiographic evidence of spinal metastases?

____(Y)  5. Is there pain associated with the positive radiographic site?

____(Y)  6. Was the radiographic study performed within 4 weeks prior to registration?

____(Y)  7. Is there impending fracture or evidence of compression fracture at the treatment site?

____(N)  8. Is surgical fixation/intervention of the treatment site planned?

____(N)  9. Has the treatment site received prior radiation therapy?

____(N)  10. Has there been surgical intervention at the planned treatment site performed in the past?

____(N)  11. Has the patient received any systemic radioisotopes within the past 30 days?

____(Y/N)  12. Is the patient currently receiving systemic treatment, i.e. chemotherapy, hormonal therapy, immunotherapy, or other investigational drugs?

____(Y)  a. If yes, can the systemic therapy be held within two weeks prior to treatment procedure?

____(N)  13. Is there clinical or radiographic evidence of spinal cord compression or cauda equina effacement?

____(Y)  14. For peri-menopausal female patient, has a pregnancy test has been done within the past 7 days with a negative result?
Due to the steep dose fall-off, a high dose to the vertebral lesion can be delivered, with maximum sparing of spinal cord. A radiation dose of 8 Gy at a distance of 5 mm from the applicator surface will be prescribed. This correlates to an approximate dose of 91 Gy at the applicator surface, 45 Gy at a distance of 1 mm (from the applicator surface), 27 Gy at 2 mm, and 8 Gy at 5 mm (Wenz F). Further dose fall off is approximated: 2.4 Gy at 10 mm, 0.8 Gy at 15 mm, and 0.4 Gy at 20 mm (Schneider F). Assuming minimal distance of 15 mm to the spinal cord, then, the spinal cord would receive less than 1 Gy.

2.5 Study Design

The combination of intraoperative radiotherapy with kyphoplasty will provide immediate vertebra stabilization, durable pain relief, and sterilization of tumor cells in a single outpatient procedure. To this date, this procedure has not been performed in the United States. We plan to conduct a phase I trial of Kypho-IORT at the Loyola University Medical Center.

3. PATIENT SELECTION

3.1 Eligibility Criteria

- Metastatic patients from solid tumor
- Estimated life expectancy of at least 3 months
- Age ≥ 50 years.
- Karnofsky Performance Status ≥ 70%
- Numeric Pain Intensity Score ≥ 3
- 10% or more loss of vertebrae height
- Adequate organ and marrow function as defined below:

  - INR/PT within normal institutional limits
  - leukocytes ≥ 3,000/mcL
  - absolute neutrophil count ≥ 1,500/mcL
  - platelets ≥ 100,000/mcL
  - total bilirubin within normal institutional limits
  - AST(SGOT)/ALT(SPGT) ≤ 2.5 X institutional upper limit of normal
  - creatinine within normal institutional limits

- Ability to understand and the willingness to sign a written informed consent
3.2 Exclusion Criteria

- Patients who have had prior external beam radiotherapy or surgery in the area of planned intervention
- Previous radiopharmaceuticals (i.e., Ra-222, Sr-90, etc) within 30 days of procedure
- Patients who are receiving systemic therapy (chemotherapy, hormonal, immunotherapy, bisphosphonates, etc) or other investigational agents are eligible if the systemic therapy can be safely held two weeks prior to procedure. These therapies may be resumed two weeks after the procedure
- Primary hematologic malignancies
- Patients with clinical or radiographic evidence of spinal cord or cauda equine compression or effacement
- Chronic vertebral fracture of greater than 6 months or coexisting bilateral pedicle fracture
- Previous kyphoplasty in the same area
- Patients with severe spinal deformity requiring open reconstruction or extreme adiposity, in which determining placement of metal sleeve would be difficult by fluoroscopy (limited bone margin)
- History of allergic reactions attributed to compounds of similar composition to agents used for kyphoplasty
- Uncontrolled medical illness including, but not limited to, ongoing or active infection, symptomatic congestive heart failure, unstable angina pectoris, cardiac arrhythmia, or psychiatric illness/social situations that would limit compliance with study requirements
- Pre-menopausal female