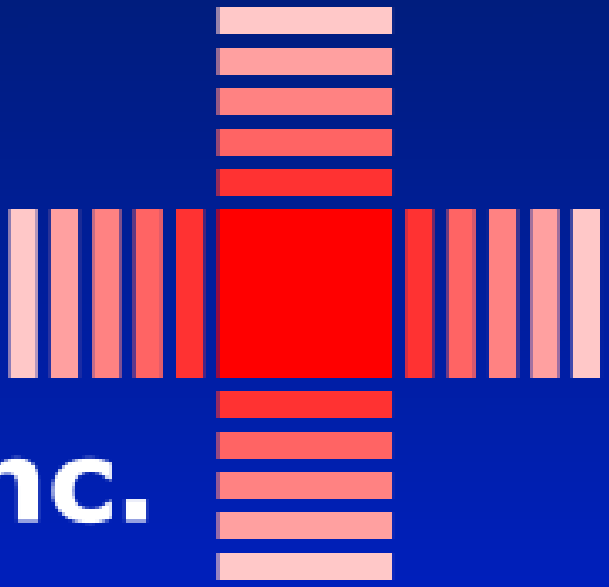
Bone-Rad Therapeutics, Inc.



a revolutionary treatment paradigm for cancer tumors in bone

Harry Skinner, MD, PhD: President/CEO, hskinner@hskinner.net, (949) 939-5132

Joyce Keyak, PhD: Principal Investigator, jhkeyak@uci.edu, (714) 423-5871

Overview

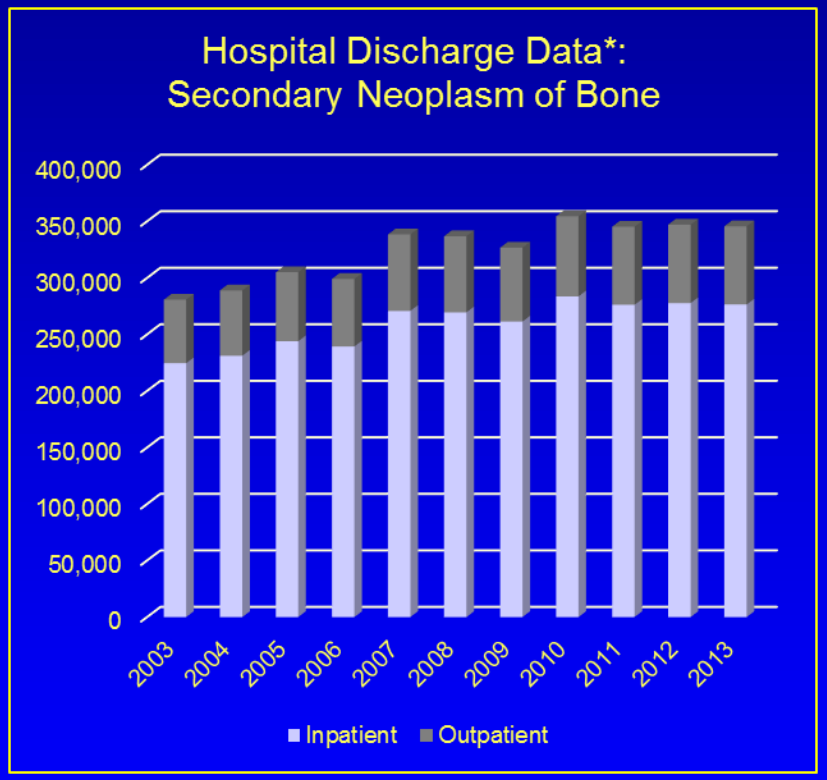
- Bone-Rad Background
- Market
- Technology
- Product and Manufacturing
- R&D / Testing
- Intellectual property
- Regulatory
- Commercialization
- Budget & Financials
- Long-Term Goals

Bone-Rad Therapeutics Co-Founders

- Joyce Keyak, PhD – Inventor, Principal Investigator
  - Biomedical/mechanical engineer
- Harry Skinner, MD, PhD – Inventor
  - Orthopaedic surgeon, materials scientist
- Varun Sehgal, PhD – Co-Principal Investigator
  - Licensed medical physicist at UCI, brachytherapy expert
- Tadashi Kaneko, PhD – Dosimetry, Business Plan Competition
  - Biomedical engineer, now at Varian

Vertebral Metastases

- > 400,000 patients / yr. with skeletal metastases
- 230,000 patients / yr. develop symptomatic vertebral tumors
- 75% are candidates for Bone-Rad's treatment
- Multiple vertebrae are often involved, further increasing the potential opportunity by approximately 30%



Incidence of Metastatic Bone Disease Increasing at 2.1% Per Year

*Agency for Healthcare Research and Quality, HCUP Database

Brachytherapy Bone Cement

Spine-Rad™ Cement – Bone-Rad's first product

- New first line treatment for tumors in the vertebral body
- Does not contribute to lifetime radiation dose limits of the spinal cord (P-32 beta emitter)

  Leaves all options open for future treatment
- Immediate pain relief in 85% of patients

Spine-Rad™ Brachytherapy Bone Cement

Conventional Treatment versus

Spine-Rad™ Treatment

Current Management of Vertebral Tumors

- External beam radiation therapy (EBRT)
  - EBRT is delayed to avoid radiation to spinal cord
  - Cannot repeat EBRT if tumor recurs
  - Pain medication, bracing, reduced QOL
- Tumor grows
  - Increased risk of neurologic complications

- EBRT 10-20 sessions over 2-4 weeks
  - Nausea, vomiting, diarrhea, skin burns
- Bone resorption, risk of vertebral collapse

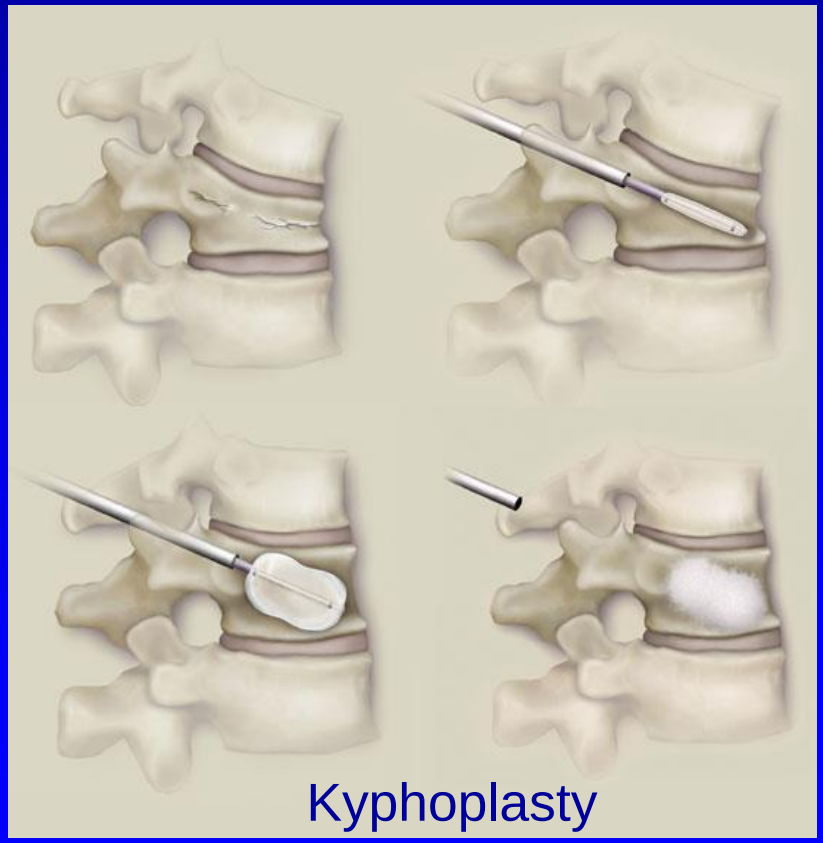
Current Management of Vertebral Tumors

- External beam radiation therapy (EBRT)
  - EBRT is delayed to avoid radiation to spinal cord
  - Cannot repeat EBRT if tumor recurs
  - Pain medication, reduced QOL
- Tumor grows
  - Increased risk of neurologic complications
- Vertebral augmentation prior to EBRT – Typically used to stabilize osteoporortic vertebral body fractures
- EBRT 10-20 sessions over 2-4 weeks
  - Nausea, vomiting, diarrhea, skin burns

Conventional Treatment of Vertebral Tumors

Step 1- Vertebral (Osteoporotic) Fracture Treatment

- Kyphoplasty
  - Minimally invasive procedure
  - Creation of void inside vertebral body
  - Injection of bone cement into void to stabilize fracture
  - Immediate pain relief in 85% of patients



Kyphoplasty

Conventional Treatment of Vertebral Tumors

Step 2- Tumor Radiation Therapy

Conventional

External Beam Radiation Therapy (EBRT)

10-20 Treatment Sessions; Significant Side Effects

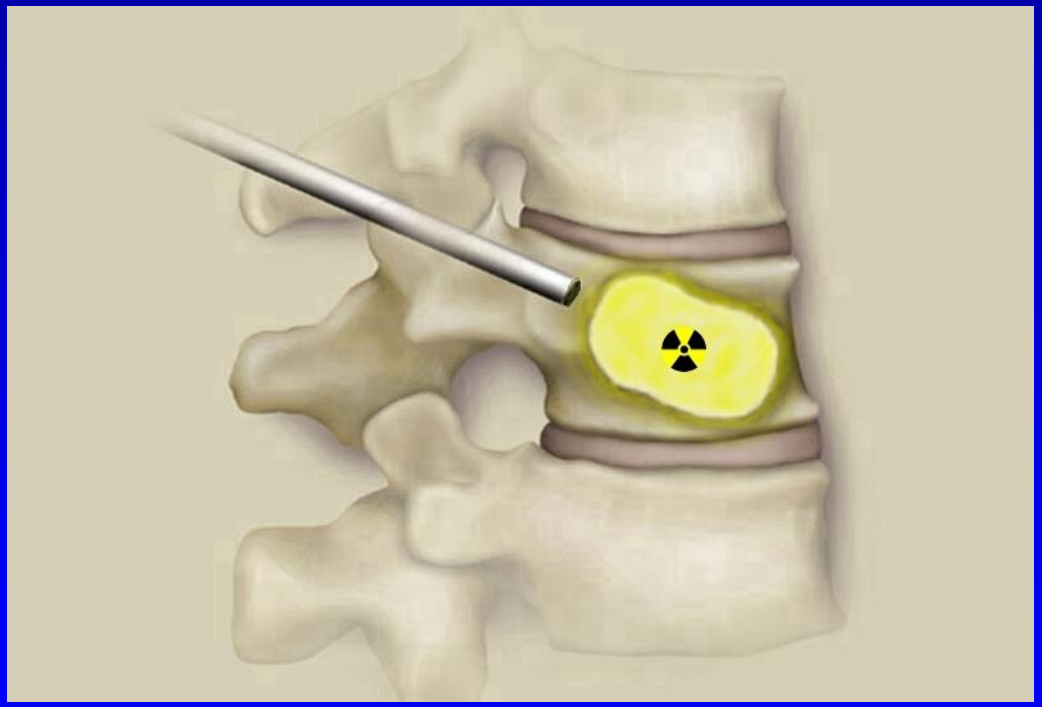
Alternative

Stereotactic Body Radiation Therapy (SBRT)

Up to 5 Treatment Sessions; Moderate Side Effects

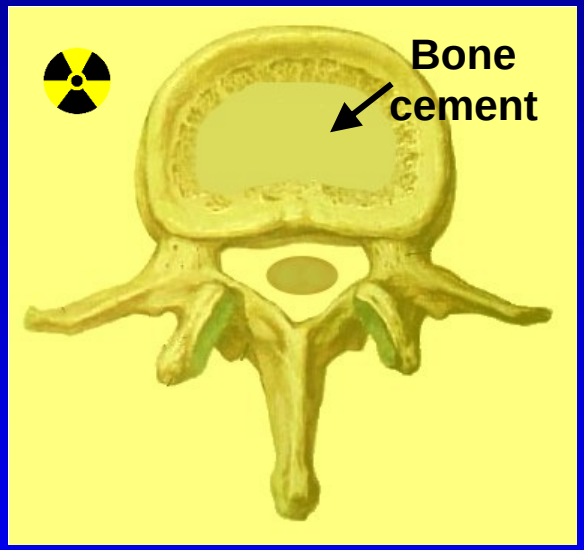
Treatment with Spine-Rad™ Cement

Spine-Rad™ Cement is Delivered Via a Standard Kyphoplasty Procedure. Commonly Performed by Thousands of Physicians Nationwide.

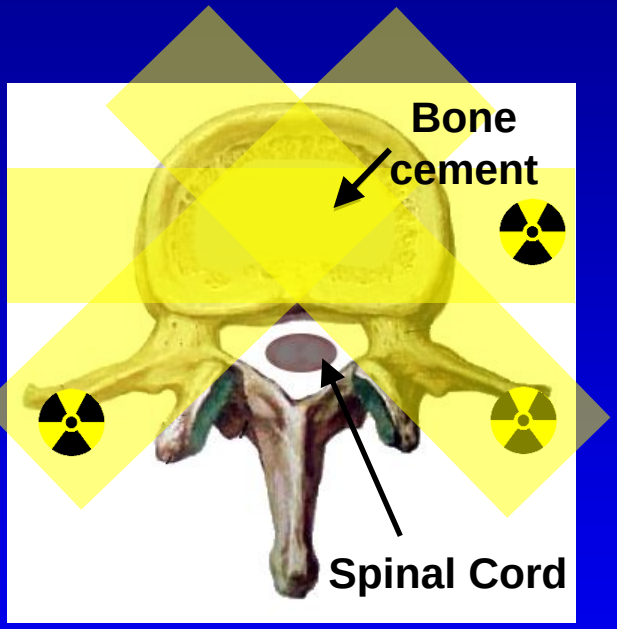


Spine-Rad™ incorporates a radionuclide into standard bone cement, allowing Spine-Rad™ Cement to irradiate the tumor internally while simultaneously preventing or repairing the fracture.

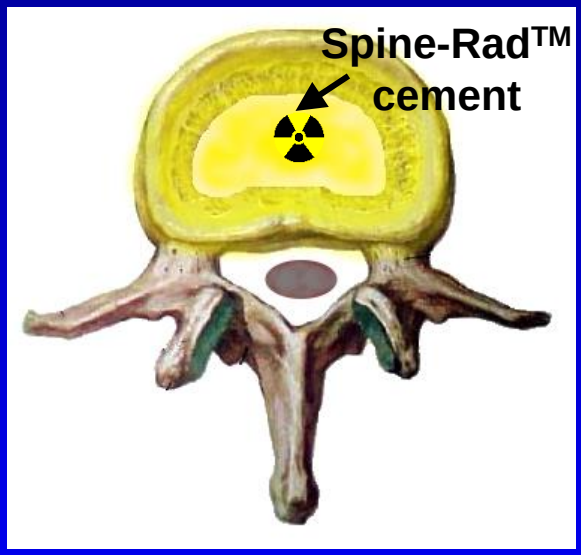
Precise Radiation Delivery Minimizes Collateral Damage



EBRT:
10-20 sessions,
exposure of spinal cord,
nerve roots, bowel, skin,
nausea, vomiting,
diarrhea, skin rash



SBRT:
Up to 5 sessions,
better targeting,
moderate side effects,
higher cost,
limited availability



Spine-Rad™:
Single procedure,
precise targeting,
no radiation side effects,
lower cost,
better QOL

Spine-Rad™ Treatment Advantages

- Allows early treatment for painful vertebral metastases because it does not irradiate the spinal cord
- Spine-Rad™ Cement combines pain relief, fracture prevention/treatment and radiation therapy into a single procedure
- None of the side effects of external radiotherapy
- One hospital visit rather than multiple visits for external radiation therapy
- Dramatic improvement in patient care and quality of life
- Subsequent external radiotherapy is still an option

Spine-Rad™ Brachytherapy Bone Cement

Product & Manufacturing

Spine-Rad™ Cement Components

All FDA-approved components

- Bone cement (acrylic powder and liquid packaged separately, then mixed)
- Hydroxyapatite (HA) – medical grade
  - Placed in nuclear reactor
  - Phosphorus becomes radioactive
  - P-32-HA

Radioisotope Supplier

- Missouri University Research Reactor
- Three FDA approved agents:
  - Ceretec: Brain Imaging
  - TheraSphere: Liver Cancer
  - Quadramet: Bone Metastases
- Continuous operation since 1977

www.murr.missouri.edu

Possible Spine-Rad™ Configurations

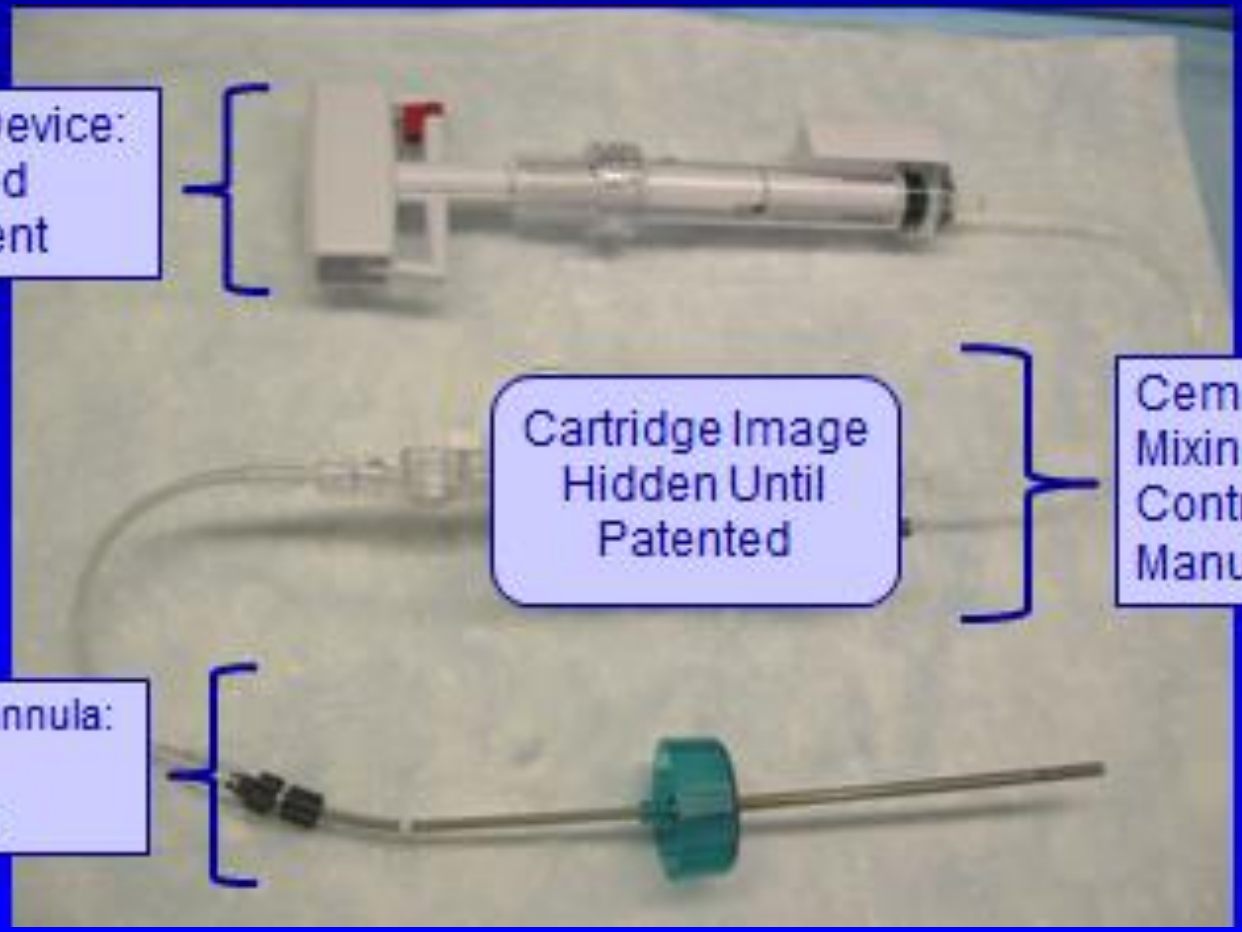
Option A

- Provide P-32-HA pre-mixed with cement powder
- Add cement liquid
- Mix
- Inject into vertebral body

Option B

- Provide P-32-HA separately
- Add cement powder and liquid
- Mix
- Inject into vertebral body

Spine-Rad™ Mixing & Delivery System Option A



Option B

- Available now for use in animal studies
- Use commercially available cement and cement mixer
- Special safety precautions and tools

Completed Feasibility Studies

- Developed and validated radiation transport model to predict dose distribution from Spine-Rad™ Cement
  - Extensive sensitivity studies
  - Unique dosimetry/properties → IP
  - Dose is independent of activity or volume of cement
- Leaching of P-32 from Spine-Rad™ Cement ex vivo is trivial
- Compressive strength of the bone cement is not affected by P-32
- Verified cement uniformity (uniform dose) from Spine-Rad™ Mixing & Delivery System

Near Future: First In Vivo Tests

Sheep – Address key questions

- Bone histology
  - Experienced veterinary orthopaedics researcher, undecalcified histology
- Determine if P-32 leaches into the bloodstream.
- Determine if sheep waste (bedding) is radioactive.
- Measure dose to personnel

UC Irvine Support and Facilities

- UCI Radiological Sciences
  - DOD funded feasibility study
  - Department support for pilot sheep study
- Animal facility at UCI
- Radiation use authorization
- Clean room facility
  - minimal cost for dedicated clean room with QA monitoring

Bone-Rad Intellectual Property

Bone-Rad – Exclusive license from the University of California

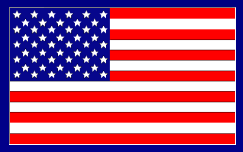
Bone Cement Patents (broad; related to dose):

- Patent No. 9,198,989 (2015) – on method of production/formulation
- Patent No. 9,597,427 (2017) – on method of treatment
- Patent No. 10,272,173 (2019) – on the material
- Patent Pending – on the material

Bone Cutting Device Patent:

- Patent No. 9,028,499 (2015)

Regulatory – FDA



Bone-Rad submitted a pre-IDE document and met with FDA panel.

The FDA has determined

- Spine-Rad is a device (not a combination product).
- Brachytherapy bone cement is a new type of device.
- Spine-Rad™ Cement should follow the PMA process.
- Spine-Rad™ is therefore a Class III device.
- CDRH Division of Orthopedic Devices will have premarket review and regulatory oversight.

Regulatory – EU

Disclaimer – this predates regulatory changes in EU:

- Spine-Rad Cement is Class II B.
- Bone Cements and Brachytherapy Devices are both Class II B.
- Due to unique nature of Spine-Rad™ a small 20 patient safety trial is required as part of CE Mark submission.
- U.S. pilot study data will be acceptable.

Spine-Rad™ Brachytherapy Bone Cement

Commercialization, Project Timeline, Budget & Financials

Please Keep in Mind:

Data and projections from 2018

- Previous CEO's goal:
  - Bone-Rad to bring Spine-Rad™ Cement to market
- Based on Bone-Rad outsourcing
- Assumes start in EU with CE Mark

Current goal:

- Partner with someone to bring this to market

Spine-Rad™ Procedure Coding:

Current Brachytherapy and Kyphoplasty Codes Apply

CPT Code	Descriptor	Hospital Outpatient Rate**	Physician Rate (PC)**
Planning and Simulation			
77263	Therapeutic radiology treatment planning; complex	-	$158.89*
77295	Therapeutic radiology simulation-aided field setting; 3-dimensional (Simulation not required for Spine-Rad)	$984.49	$226.25
72131	Computed tomography, lumbar spine; without contrast material	$173.58	$47.97
77236	Brachytherapy isodose plan; simple	$109.73	$45.93
77336	Continuing medical physics consultation	$109.73	$43.89*
Treatment Management			
77761	Intracavitary radiation source application; simple	$410.83	$189.85
77790	Supervision, handling, loading of radiation source	-	$51.37
Q3001 C2699	Radioelements for brachytherapy any type, each. Brachytherapy source, non stranded, per source	$8000*	-
Procedure			
22524	Kyphoplasty; 1 vertebral body; lumbar	$5,862.48	$537.90
77799	Unlisted procedure, clinical brachytherapy	$410.83	Carrier priced

*Carrier price based on Charge to Cost Ratio. **Medicare National Average Payment

External Beam Radiation Therapy Hospital Outpatient Treatment Reimbursement

				Private Payer Reimbursement	
Treatment	Estimated Facility Charges	Medicare Facility Payment	Medicare Physician Payment**	150% Medicare (Facility & Phys.)	70% of Billed Charges (Facility)
EBRT	$18,546	$4,428	$1,846	$9,411	$12,982
IMRT	$39,424	$9,557	$3,708	$19,898	$27,597
SBRT*	$54,807	$15,659	$3,708	$29,051	$38,365

Facility charges estimated at 4x costs.

With the exception of SBRT, actual payment rates derived from Medicare Addendum B, 2013.

* Estimated payment used for SBRT, as it is carrier priced.

** Professional Component and Technical Component (PC & TC)

Estimated Hospital Outpatient Cost of Care: Vertebral Fracture Due to Cancer

	Kypho w/ Spine-Rad	Kyphoplasty Followed By:		
		EBRT	IMRT	SBRT
Kypho Procedure / Facility	$3,200*	$3,200*	$3,200*	$3,200*
Kypho Devices	$1300*	$4,500*	$4,500*	$4,500*
Cement	Included	$400*	$400*	$400*
Spine-Rad Device	$10,200††	N/A	N/A	N/A
Radiation Therapy[10,11,13]	Included	$9,865**	$16,913††	$24,629††
Radiation Treatment Plan	$1223†	Included in Radiation Therapy Costs		
Total	$15,923	$17,965	$25,013	$32,792

* Based on $8100 total hospital costs for Kyphoplasty, Mehio AK et al., AJNR May, 2011

** Based on costs of Radiation Episode of Care references 10 & 11

Private Payer estimates based on 150% of Medicare Payments

† Planning & simulation reimbursement (prev. slide) adjusted to account for 55% Private Payers

†† Facility and physician reimbursement (prev. slide) adjusted to account for 55% Private Payers

Estimated Costs to Market
(as of 2018)

- $2MM to complete preclinical activities and submit IDE.
- An additional $3MM to get to CE Mark and EU market entry
- Total of $24MM to fund through FDA approval

Planned Clinical Study

- Evaluation of Safety & Performance
  - Delivery of therapeutic dose to tumor site
  - Minimize radiation exposure to spinal cord and nerve roots
  - Mixing and delivery system performs as indicated
- Secondary Measures
  - Pain, health and function measures
  - Tumor response
- Final protocol from pre-IDE communications with FDA
- Clinical Trial Costs
  - $10MM, Based on quote from independent CRO

Spine-Rad Project Timeline & Expenses (as of 2018)

	Year 1	Year 2	Year 3	Year 4	Year 5	Expense
Preclinical						$2,000,000
IDE & IRB's						$200,000
Pilot Study						$725,000
CE Mark & E.U. Launch						$540,000
Pivotal Study						$9,478,000
PMA Prep and Submission						$750,000
FDA Approval						$250,000
G&A/S&M/R&D/Manu						$4,575,588
Salaries & Benefits						$4,793,619
IP/Royalty						$792,930
Total	$2,000,000	$2,995,000	$6,452,880	$7,052,463	$5,604,794	$24,105,136

- **Total expense may be reduced by $2MM if a smaller pivotal study is required**
- **OUS revenues begin in year 3 and total approximately $10MM in years 3-5**
- **Margin of OUS revenues is 79% and offset expenses prior to U.S. launch**

Global Spine-Rad Sales Projections (as of 2018)

(000's)	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7
Procedures	0.1	0.54	1.1	3.3	6.6	11.2	17.6
Sales	$492	$3,246	$6,693	$23,165	$47,604	$81,825	$131,151
Gross Margin	$357	$2,429	$5,260	$19,503	$41,604	$72,944	$117,301
GM%	73%	75%	79%	84%	87%	89%	89%
Op. Expenses	$6,453	$7,052	$5,605	$9,611	$17,081	$26,421	$39,838
Pre-tax Income	($6,096)	($4,623)	($345)	$9,892	$24,523	$46,523	$77,463

- Year 1 of sales is the 3rd year after funding
- Years 1-3 are OUS only
- U.S. metrics by year 7 of sales:
  - $100MM in revenues
  - 7% market share
  - 90% gross margin
- Overall positive cash flows in the 2nd month of year 4 of sales

Bone-Rad Market Comparables

Spinal Dynamics, Inc. (disc replacement device)

- 1997-2001: Four rounds of funding
- May 2002: IDE and clinical study
- October 2002: Purchased by Medtronic for $270M

St. Francis Medical (spinal fusion device)

- November 2005: FDA approved
- January 2007: Purchased by Kyphon for $525M (8.5x revenues)

Kyphon, Inc. (Spinal devices/ Kyphoplasty)

- 1994: Company founded
- May 2000: Balloon kyphoplasty approved
- July 2007: Acquired by Medtronic for $3.9B (8x revenues)

SenoRx, Inc. (Breast cancer diagnostics and brachytherapy)

- August 2008: brachytherapy device approved
- May 2010: Acquired by CR Bard for $200M (4x revenues)

Bone-Rad Market Comparables

Blackstone Medical, Inc.

- Stem cell biologic products for bone growth & spinal fixation hardware devices.
- 2003, sales exceeded $40M, and in 2006 exceeded $90M.
- Acquired in 2006 by Orthofix International N.V. for $333M, a 3.7x revenue multiple.

Endius, Inc.

- Minimally-invasive spine surgery products and implants to treat serious spine disease
- FDA 510(k) clearance in October 2000.
- Acquired in 2007 by Zimmer Holdings, Inc. for an unspecified amount.

Spinal Concepts, Inc.

- Medical devices used during spinal fusion surgical procedures.
- FDA 510(k) clearance in 1998 for its BacFix® pedicle screw
- Sales for 2001 exceeded $15M and tripled to $45M by 2003
- Acquired by Abbott Laboratories for $170M in cash.

Bone-Rad Summary

- Spine-Rad™ Cement allows early treatment for painful vertebral metastases because it does not irradiate the spinal cord
- Brachytherapy, with no external beam radiation side effects
- Improved patient care and QOL at lower cost
- Standard kyphoplasty – minimizes training and facilitates adoption
- No capital equipment – allows Spine-Rad™ to be widely available
- Simple dosimetry
- Intellectual property established and growing (novel technology)
- Existing brachytherapy and kyphoplasty reimbursement codes apply
- Large, growing market

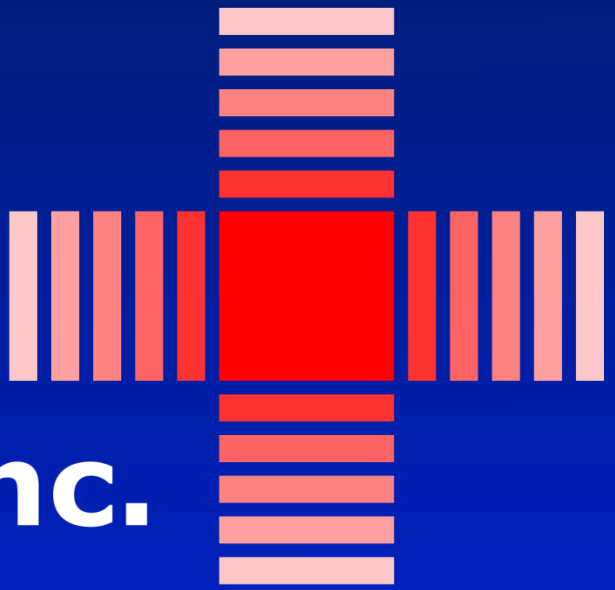
Long-Term Goals

- Partner with someone to bring this to market
- Dr. Keyak is available to facilitate
  - Product development
  - Establishment of new IP (e.g. breast cancer treatment)
- Bone-Rad has access to other experts

Bibliography

1. American Cancer Society; Cancer Facts and Figures 2013.
2. Coleman RE., et. al. Advancing Treatment for Metastatic Bone Cancer: Consensus Recommendations from the Second Cambridge Conference..., Clin. Cancer. Res. 2008
3. Mundy GR. Metastasis to Bone: Causes, Consequences and Therapuetic Opportunities; Nature Reviews, 2002.
4. Wong et al., Spinal Metastases: The Obvious, the Occult and the Imposters., Spine v.15 no.1, 1990
5. Gokaslan et al., Transthoracic Vertebrectomy for Metastatic Spinal Tumors, J. Neurosurgery 89; 599-609, 1998
6. Rose & Buchowski; Metastatic Disease in the Thoracic and Lumbar Spine; Evaluation and Management, J. Am. Acad. Ortho. Surg., 19; 37-48, 2011
7. Healthcare Cost and Utilization Project and National Hospital Discharge Survey
8. Mariotto AB, Yabroff KR, Shao Y, Feuer EJ, Brown ML. Projections of the Cost of Cancer Care in the U.S.: 2010-2020. *J Natl Cancer Inst*. 2011 Jan.
9. Schluman KL. & Kohles J., Economic Burden of Metastatic Bone Disease in the U.S., American Cancer Society 2007.
10. Hagiwara M. et al., Healthcare Utilization and Costs Associated with Skeletal-Related Events in Prostate Cancer Patients with Bone Metastases.
11. Hess G. et al., Costs of Palliative Radiation to the Bone for Patients with Bone Metastases Secondary to Breast or Prostate Cancer., Radiation Oncology 2012, 7:168.
12. Mehio AK et al., Comparative Hospital Economics and Patient Presentation: Vertebroplasty and Kyphoplasty for the Treatment of Vertebral Compression Fracture, AJNR May, 2011
13. Medical Technology Partners, TrueData Report, Incidence and Costs Associated with EBRT, IMRT and Cyberknife to Treat Spine Tumors, 2009

Bone-Rad Therapeutics, Inc.



a revolutionary treatment paradigm for cancer tumors in bone

www.bone-rad.com

jhkeyak@uci.edu

hskinner@hskinner.net