

# PALLIATIVE RADIOTHERAPY FOR SKELETAL-RELATED EVENTS IN NEUROENDOCRINE NEOPLASMS

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## Background

- Bone metastases have been reported in up to 12% of patients with neuroendocrine neoplasms (NENs). These metastases can lead to pain and other skeletal-related events (SREs) resulting in diminished quality of life and functional status.
- In other solid tumors, radiotherapy is an established treatment approach for SREs. We hypothesize that radiotherapy is an effective therapy for pain and other SREs in patients with NENs.

## Methods

- We reviewed 686 records of consecutive NEN patients treated at Cedars-Sinai Medical Center between 2011 to 2018 to identify patients with NENs who underwent radiation for bone metastases.
- The primary endpoint was change in patient reported pain scores following radiotherapy. The secondary endpoint was time to recurrence or progression of pain.

## Results

- 28 patients (ages 35-88 years) with NENs treated for 61 cases of SREs were identified.
  - There were 11 lung NENs (7 typical carcinoids, 2 atypical carcinoids, 1 large cell, 1 small cell NEN) and 18 non-lung NENs (8 low, 8 intermediate, and 1 high grade NEN).
  - 7 patients received 1 line of systemic therapy, 19 patients received 2 or more lines, and 2 patients received no systemic therapy.
  - All 28 patients experienced bone pain, 7 patients experienced neurological compromise and 9 patients experienced impending or pathologic fractures.
  - 19 sites were treated with single fraction doses of 800-1800 cGy and 34 sites were treated with fractionated regimens (doses of 900-3750 cGy over 3 to 15 fractions).
- In 56/61 (92%) cases, patients experienced improvement in pain scores following radiotherapy.
  - Median time to recurrence or progression of pain was 3.5 months.
  - Outcomes were similar for patients who received single fraction vs fractionated regimens ( $p=0.545$ ) in this cohort.

Table 1. Demographics

Gender, n (%)	
Female	15 (53.6%)
Male	13 (46.4%)
Primary tumor site, n (%)	
Pancreas	7 (24.1%)
GI tract	4 (13.8%)
Lung	9 (31.0%)
Other	7 (24.1%)
Unknown	2 (6.9%)
Grade, n (%)	
GI tract	
G1	8 (27.6%)
G2	8 (27.6%)
G3	1 (3.4%)
Lung	
Typical	7 (24.1%)
Atypical	2 (6.9%)
Large Cell	1 (3.4%)
Small Cell	1 (3.4%)
Unspecified	1 (3.4%)

Table 2. Treatment of SREs

Site of radiation, n (%)	
Axial Skeleton	48 (77.4%)
Appendicular Skeleton	9 (14.5%)
Both	4 (6.5%)
Type of radiation therapy, n (%)	
Single fraction	20 (32.3%)
Fractionated	42 (67.7%)
Response to radiation, n (%)	
Improvement	56 (91.9%)
No response	2 (3.2%)
Response not documented	2 (3.2%)
Did not complete treatment	1 (1.6%)
Time to recurrence, n (%)	
No recurrence	20 (35.7%)
≤ 2 months	17 (30.4%)
> 2 months	19 (33.9%)
Other SREs, n (%)	
Neurologic Compromise	7 (11.3%)
Impending or Compression Fracture	9 (14.5%)
No other SREs	46 (74.2%)
Other treatments for SRE, n (%)	
None	18 (64.2%)
Surgery	4 (14.3%)
Zometa	1 (3.6%)
Denosomab	3 (10.7%)
Surgery and Zometa	1 (3.6%)
Surgery and Denosomab	1 (3.6%)



Figure 1. A 63-year-old male with primary NEN of the pancreas with bony metastases involving the left pelvis and sacrum. He experienced significant pain which improved following radiation with 2500 cGy delivered in 5 fractions. MRI of the sacrum demonstrates extensive bone metastases involving the superior central part of the left iliac bone and flanking the left sacroiliac joint.

## Conclusion

A significant portion of patients with NENs who experienced SREs from metastases demonstrated improvement in bone pain following radiotherapy. Further studies are needed to determine the role and optimal schedule of radiotherapy in the treatment of bone metastases.