

PALLIATIVE RADIATION EVIDENCE BASED APPROACH



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Why this topic?

- A recent article by Dr. Aileen Chen of the Dana-Farber Cancer Institute in Boston showed that in patients with terminal lung cancer two-thirds did not understand that treatment was not likely to cure them.¹⁰
 - ▣ 5,013 patients were newly diagnosed with lung cancer between 2003-2005
 - 832 had stage IIIb or IV and were due to undergo radiation therapy.
 - 384 (46%) of this completed surveys about their beliefs about the therapy.
 - ▣ 19% said it was very likely and 24% said it was somewhat likely that radiation therapy would actually cure their cancer
 - ▣ Seventy-eight percent believed radiation was "very" or "somewhat" likely to help them live longer.

What is palliative radiation?

- According to National Cancer Institute palliative radiation treatments are **not** intended to cure. Instead, they **relieve symptoms** and **reduce suffering** cause by cancer. ²



Background

- In North America and Europe, approximately 45-50% of patients with cancer receive radiation therapy at some time during the course of their disease. ³
- ▣ Approximately half of this prescribed radiotherapy is given for palliation of symptoms due to incurable cancer.
- ▣ Most of the patients prescribed for palliative radiation are the ones with pain, bleeding or obstruction which can have relief with minimal toxic effects.

Goals of palliative radiation:

1. To achieve meaningful relief of symptoms
2. To use treatment that reconciles patient inconvenience in the context of limited survival time with the need for palliation that is as complete and durable as possible
3. To administer therapy with negligible or mild toxic effects.

Keep in mind...

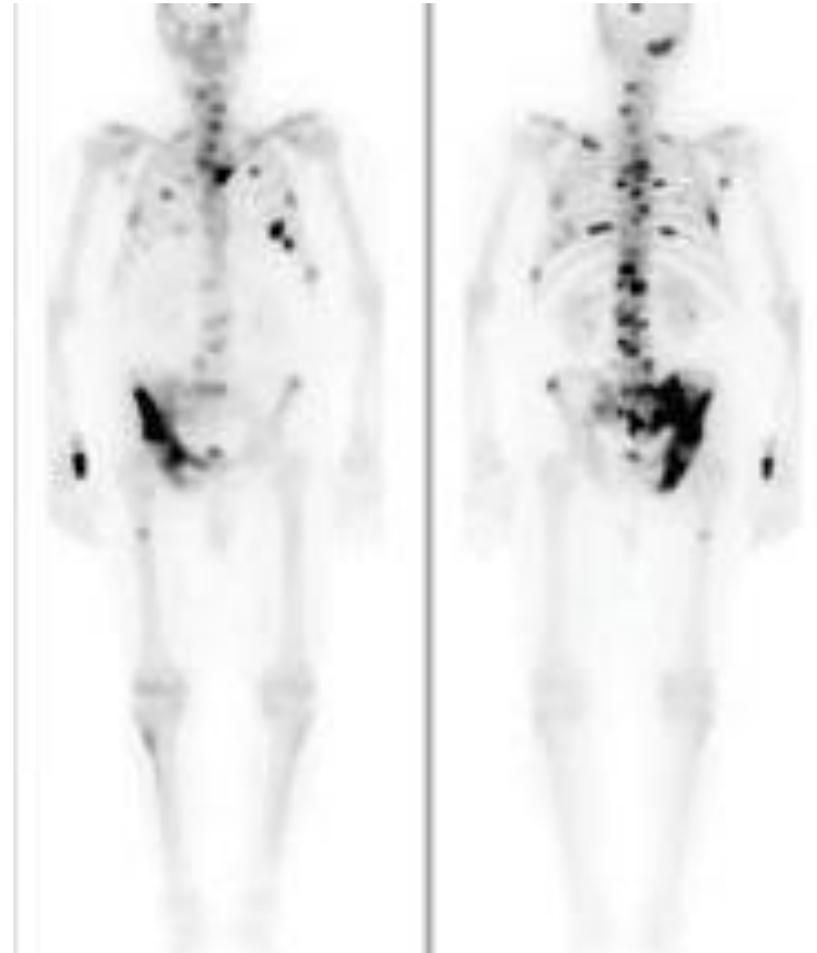
- In curative RT the goal is to deliver a high total dose to the tumor while limiting long-term toxicity to normal tissues
 - ▣ This is achieved by dividing the treatment into high number of low-dose fractions.
 - ▣ This results in long overall treatment course usually requiring 7-8 weeks of treatment
- In palliative RT, shorter overall treatment times are desirable because they offer low cost and greater convenience, with fewer daily trips, which are of particular burden in the face of short life expectancy.
- Some definitions:
 - ▣ Fraction:
 - A single treatment session
 - Conventionally 1.8 – 2.0 Gy
 - Hypofractionation:
 - Fewer fractions than conventional with higher dose per fraction.
 - Shorter treatment time.
 - Slight increased probability of late effects.

Indications of Palliative RT

- Pain relief from bone metastasis
- Prevention of pathological fractures
- Spinal cord compression.
- Impending or actual obstruction hollow viscera.
- Brain mets.
- Control of Haemorrhage.
- Control of ulceration/fungation.

BONE METASTASIS

- Common manifestation of malignancy that can cause severe and debilitating effects, including pain, spinal cord compression, hypercalcemia, and pathologic fracture. ⁵
- RT can provide significant palliation of painful bone metastases in 50–80% of patients
 - ▣ Up to one-third of patients achieving complete pain relief at the treated site



Treatment Recommendations

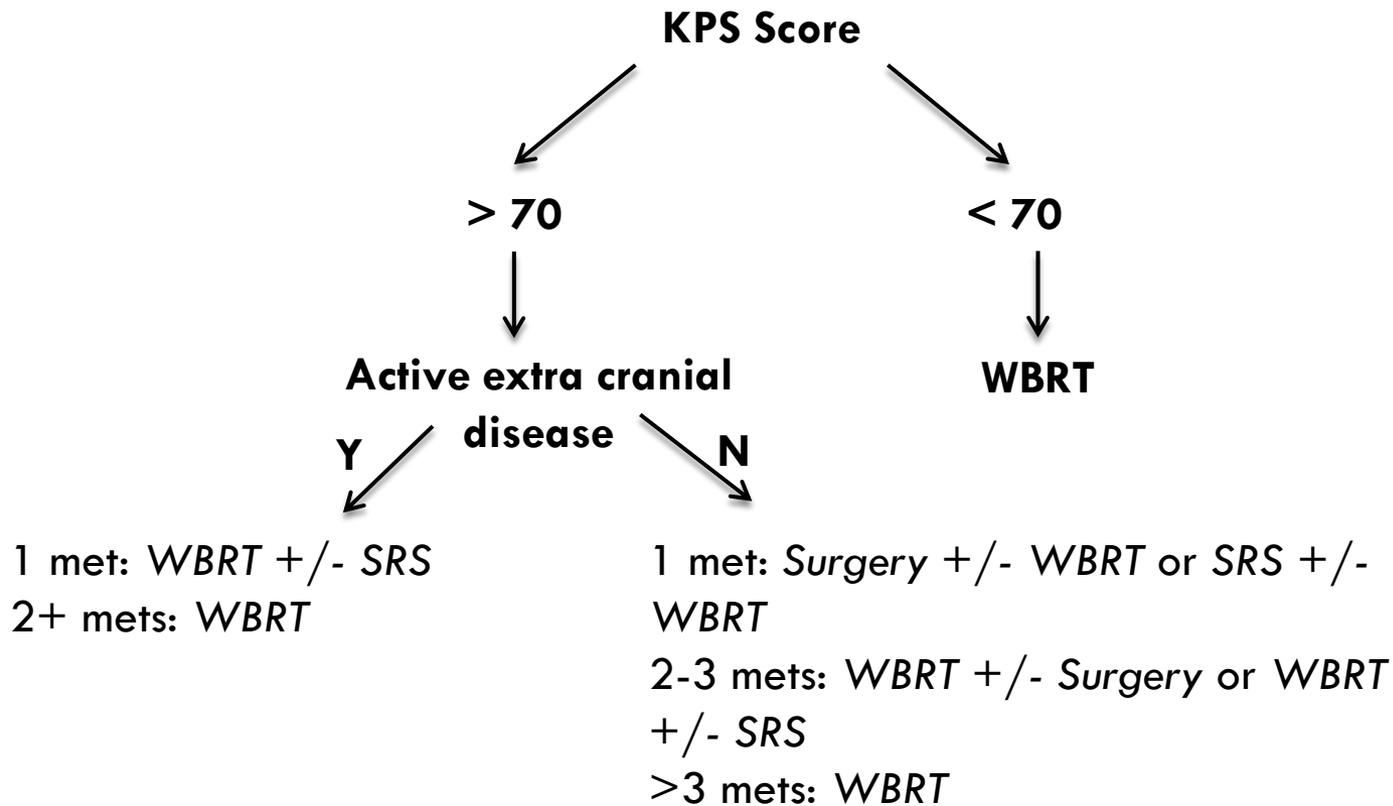
- Systematic review of 25 randomized controlled trials comparing single fraction Vs multiple fractions.
 - ▣ Trials included 30 Gy in 10 fractions, 24 Gy in 6 fractions, 20 Gy in 5 fractions, and a single 8-Gy fraction
 - ▣ Overall and complete response rates were similar in all samples.
 - ▣ Endpoints using pain relief, narcotic relief and quality of life measures show consistent similarity in the regimens
 - ▣ Fractionated RT courses have been associated with an 8% repeat treatment rate to the same anatomic site because of recurrent pain vs. 20% after a single fraction
 - however, the single fraction treatment approach optimizes patient and caregiver convenience ^{4, 5}

BRAIN METASTASIS

- Incidence:⁶
 - Estimated 170,000 - 200,000 new cases in US per year
 - On autopsy, ~10-30% of cancer patients have brain metastases
 - Lung cancer 34%, breast cancer 30%, melanoma 72%



Treatment Recommendations

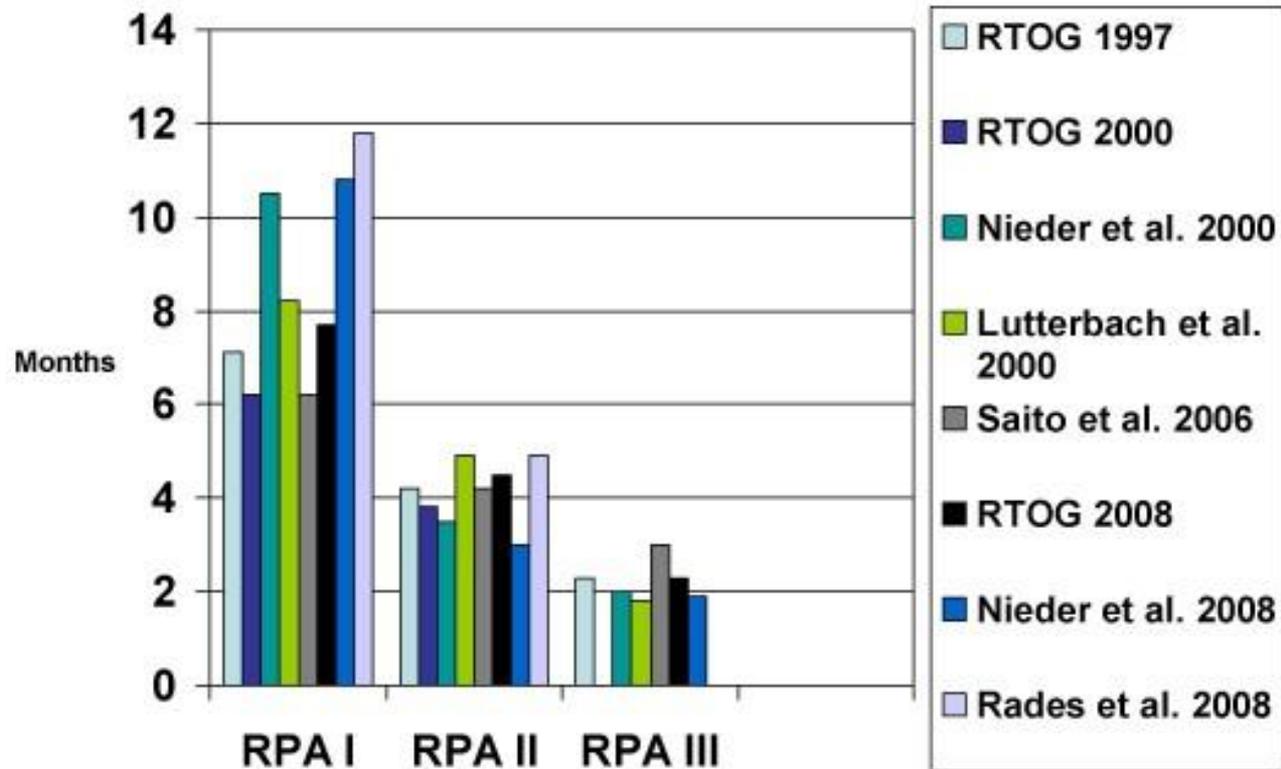


Prognostic Factor

- Recursive partitioning analysis (RPA)

RPA Stages For Brain Metastases

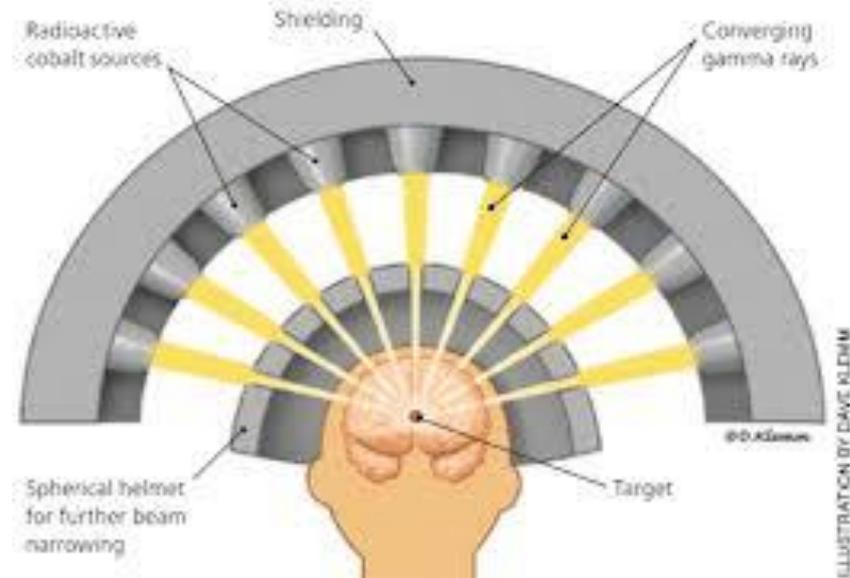
Stage	Characteristics	Median Survival (mo)
I	KPS \geq 70, age <65, primary controlled, no other extracranial mets	7.1
II	all others	4.2
III	KPS <70	2.3



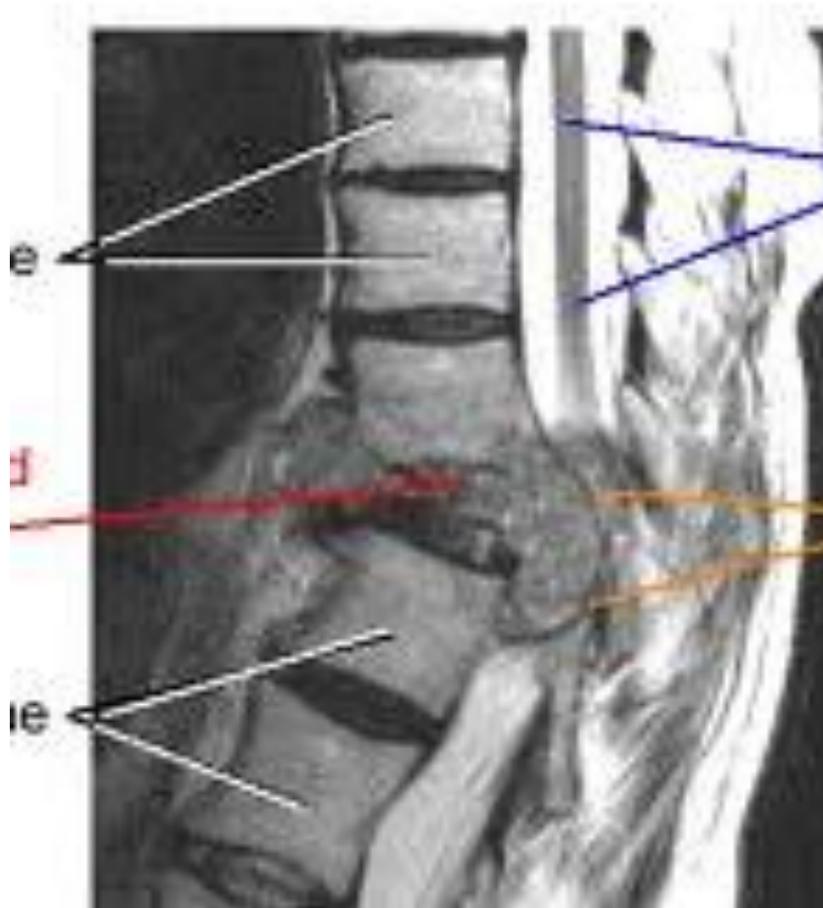
Comparison of median survival in 7 studies using the recursive partitioning analyses (RPA) classes (treatment was WBRT with or without local measures, none of the studies is limited to one particular cancer type).

WBRT + SRS Vs WBRT alone

- Analysis of all included patients, SRS plus WBRT, did not show a survival benefit over WBRT alone. However, performance status and local control were significantly better in the SRS plus WBRT group. Furthermore, significantly longer OS was reported in the combined treatment group for RPA Class I patients as well as patients with single metastasis.

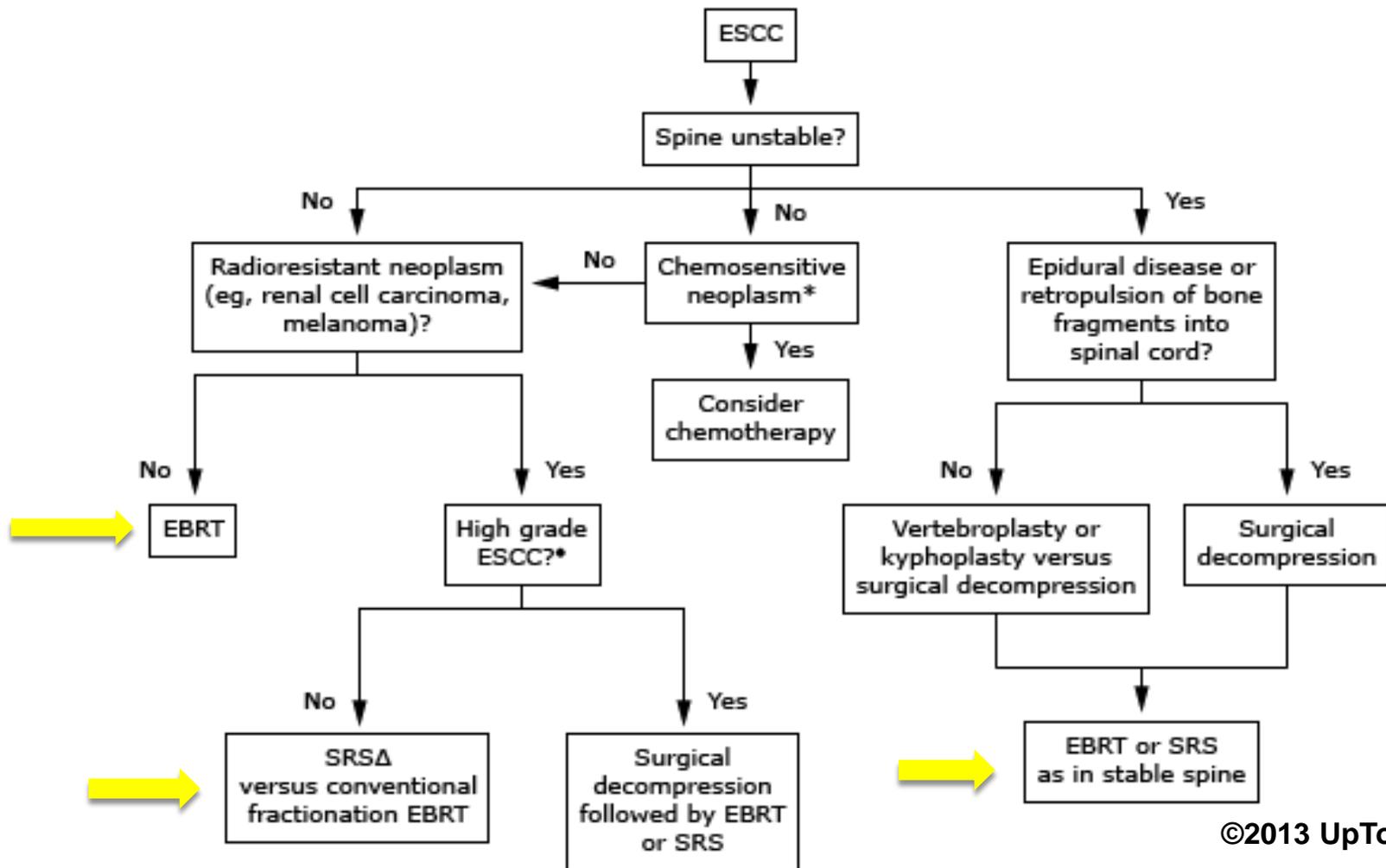


Spinal Cord Compression



- Incidence:
 - can develop in ~5-10% of patients with cancers and is one of the most debilitating complications.
 - Breast, lung, and prostate cancer are the most common malignancies causing this complication in the United States.
- Location:
 - 95% of the cases have an epidural location with both compression on ipsilateral and contralateral cord.
 - In many cases there is concomitant vertebral body involvement with growth into epidural space.

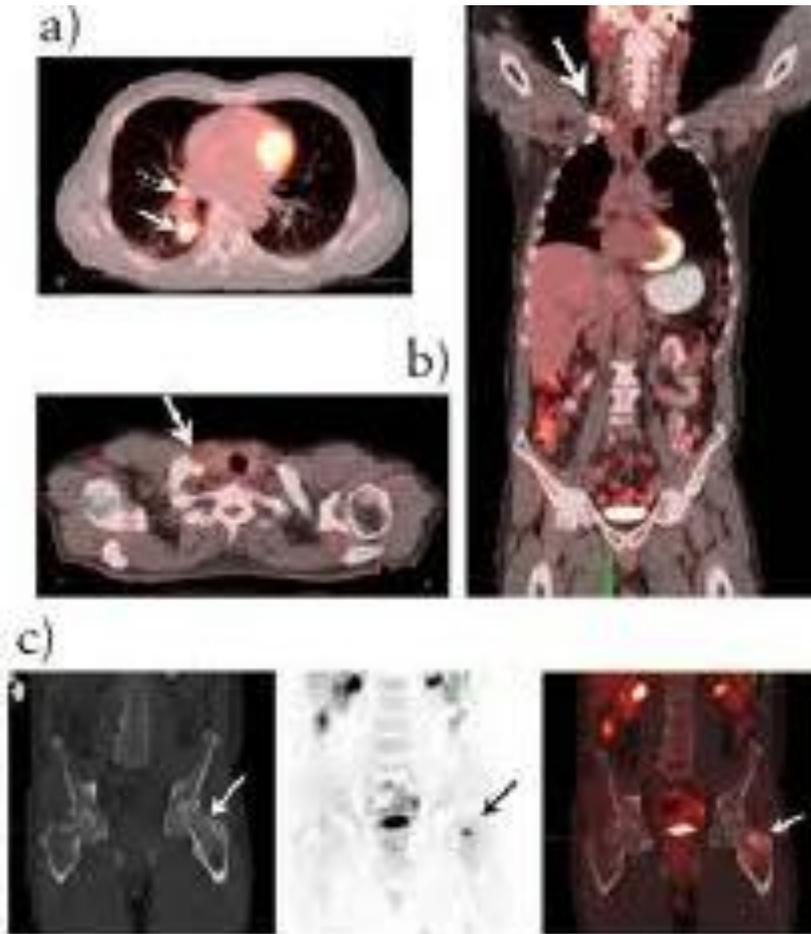
Treatment



Radiotherapy Recommendations

- An optimal dose fractionation schedule or optimal standard dose for treatment has not been established.
 - ▣ Final treatment decisions are left to provider. In making the decision it is important to keep in mind different therapeutic goals. Some options of fractionation schedules include:
 - $1 \times 8 \text{ Gy}$, $5 \times 4 \text{ Gy}$, $10 \times 3 \text{ Gy}$, $15 \times 2.5 \text{ Gy}$, $20 \times 2 \text{ Gy}$
- Things to consider:
 - ▣ Short-course radiotherapy be administered to patients with spinal cord compression and short life expectancy.
 - ▣ Long-course radiotherapy be administered to patients with inoperable spinal cord compression and good life expectancy.

Locally Advanced Lung Cancer



- About 50% of patients with non-small cell lung cancer have metastatic disease at time of diagnosis.
- Radiation therapy in this setting is NOT curative but meant to palliative symptoms from local and distant metastasis.

Evidence behind palliative RT for lung cancer¹

- Several meta-analysis, including 14 randomized studies, found the following:
 - ▣ Shorter, lower dose RT courses (10 to 35 Gy in 1 to 10 daily or 16 twice daily fractions) result in **equivalent** palliation of specific symptoms with less treatment related dysphagia.
 - ▣ Higher doses (17 to 60 Gy in 2 to 30 fractions) were associated with **small improvement** (27% to 22%) in one year survival.
 - ▣ Given heterogeneity of studies **optimal dose is unknown**
 - Secondary analysis of data showed slight benefit with a biologically effective dose of 35 (roughly 30Gy in 10 treatments) compared with lower doses.

CanCORS Study Results¹

- 1,574 patients with metastatic NSCLC
 - ▣ 780 (50%) received at least 1 course of RT.
 - ▣ The most common sites radiated were brain 22%, chest 21% and bone 12 %.
- Of the patient receiving palliative RT:
 - ▣ Bone:
 - 50% of patients had 6-10 treatments. Only 6% received a single fraction (despite evidence suggesting that this is enough for palliation)
 - ▣ Chest:
 - 65% of patients received more than 30 Gy and 33% received more than 50 Gy, which exceeds the levels showing therapeutic benefit as evaluated in almost all clinical trials.
- Patients treated in integrated networks were more likely to receive lower doses and fewer fractions.

PALLIATIVE RADIOTHERAPY

Some of the issues with the evidence

- Despite the evidence available, some providers continue to believe that higher total dose and fractionation are preferred
 - ▣ They may believe that higher doses can be delivered with only minimal toxicity and fail to take into account time, cost and convenience to patients which should play an even bigger role in a palliative approach.
- Providers may also be overly optimistic and have difficulty talking about prognosis to patients which in turn changes patients expectations and makes them more likely to agree with more difficult regimens.¹⁰
- Studies about palliative RT do not always have quality of life measures as an endpoint which makes it difficult to assess the effects of different radiation regimens and if they are truly working for the benefit of these patients.

Measuring QOL

- The European Organization for Research and Treatment of Cancer (EORTC) addressed the need for standardized QOL tools by coordinating the development of both a generalized QOL questionnaire and disease-specific QOL questionnaires (ex QLQ-LC13 is specific to lung cancer)
 - ▣ **EORTC QLQ-C30 – 30 questions**
 - ▣ **EORTC QLQ C15** is a questionnaire developed to assess the quality of life of palliative cancer care patients

Quality of Life in Patients Treated with Palliative Radiotherapy for Advanced Lung Cancer and Lung Metastases ¹¹

- Thirty-one patients with advanced lung disease were included.
 - ▣ 61% of participants were male and 39% were female.
 - ▣ Median age was 69 years (range 38 - 85), and median KPS and PPS scores at baseline were both 70 (range 30 - 90).
 - ▣ All patients received radiotherapy to the lung.
- None of the QLQ-LC13 (lung cancer specific) scores significantly improved or deteriorated at any follow-up.
- QLQ-C15-PAL scales, fatigue, pain, insomnia and physical functioning significantly improved at their respective follow-ups.

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