Radiation Therapy Approaches in the Elderly

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Introduction

• Main Interests: Stereotactic Radiosurgery (SRS), Stereotactic Body Radiation Therapy (SBRT/SABR), Neuro-oncology
  Other sites: Breast, Urological Malignancies

• Concerning RT in Geriatric Patients:
  ‘Level I evidence in older patients is limited’ ; ‘under-represented in clinical trials and extrapolation of randomized controlled trial (RCT) results to older patients is not straightforward’
Introduction

• Review of current best practice and priorities for research in radiation oncology for elderly patients with cancer: the International Society of Geriatric Oncology (SIOG) task force. Kunkler IH et al

• NCCN guidelines on ‘Senior Adult Oncology’

• Provide a broad overview of practical Radiation Oncology approaches in Geriatric Patients

• Offer range of Radiotherapeutic Options available for the individualized management of elderly patients
Scope

- Big Picture Concepts
- Radiation Therapy Approaches
- Clinical Recommendations
- Future Directions and Conclusion
As a non-invasive local therapy, RT can be delivered ‘easily’ to elderly patients. We can vary the dose, no. of fractions, size of the field, complexity of technology to fit the particular situation. Question is what are we looking to achieve?

- Trial Design and Generalizability
- Chronological Age, Co-morbidities, Functional Status
- Patient Factors, Disease Factors, Treatment Factors
- Under-treatment vs Over-treatment
- Issue of Metrics: Outcomes (Quantity/Quality) vs Cost
Radiation Therapy Approaches

- 1/2D
- 3D
- IMRT
- IGRT
- ‘4D’
- STEREOTACTIC (SRS/SBRT-SABR)
- Proton Therapy
Radiation Therapy Approaches
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## Radiation Therapy Approaches

<table>
<thead>
<tr>
<th></th>
<th>Conventional RT</th>
<th>SBRT</th>
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<tbody>
<tr>
<td>Planning</td>
<td>Relatively Simple</td>
<td>Complex</td>
</tr>
<tr>
<td>Duration</td>
<td>25-35#, Up to 7 wks</td>
<td>1-5#, Up to 5 days</td>
</tr>
<tr>
<td>Field</td>
<td>Wider</td>
<td>Conformal</td>
</tr>
<tr>
<td>Dose</td>
<td>Low (2-2.75 Gy)</td>
<td>Severe Hypo#, High (6-24Gy)</td>
</tr>
<tr>
<td>Toxicity</td>
<td>Higher, Transient</td>
<td>Low, Potentially Serious</td>
</tr>
<tr>
<td>Retreatment / Overlap</td>
<td>Not Possible</td>
<td>Possible</td>
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Radiation Therapy Approaches

- Standard Fractionation
- Hypofractionation
- Ablative
- Curative, Adjuvant, Palliative, Ablative
Radiation Therapy Approaches

Summary

- Technology improves dosimetry (conformality, homogeneity)

- Improved dosimetry reduces normal tissue coverage

- Reduced normal tissue effects: Less toxicity, Ability to Dose escalate

- Dose Escalation = More Options
Radiation Therapy Approaches

Summary

• Modality specific level 1 evidence lacking

• More so in the realm of geriatric oncology

• Cost benefit issues dominate the conversation!
SIOG recommendations for standard RT in the Elderly: Prostate Cancer

- **Patients with low-risk PC**

- Management selection (HT, watchful waiting, EBRT, BCT or surgery) should be based on geriatric assessment.

- Significant comorbidity should be a strong relative contraindication to aggressive treatment.
SIOG recommendations for standard RT in the Elderly: Prostate Cancer

- Patients with intermediate or high-risk PC

- Patients with no or mild comorbidity have a significant OS benefit from short-course ADT added to EBRT. In men without moderate or severe comorbidity six months of hormones added to EBRT should be proposed.

- For high-risk PC, CMT with EBRT and long-term ADT should be indicated after selection based on geriatric evaluation and treatment tolerance.
SIOG recommendations for standard RT in the Elderly: Prostate Cancer

- **EBRT technique in elderly**

- 3D-EBRT is recommended for all patients. IMRT is generally associated with less grade-3 proctitis, compared with 3D-EBRT.

- Shortened, hypofractionated RT may be a more convenient alternative in elderly patients.

- The role of BCT in elderly patients with low-risk PC should be defined in prospective studies taking into account life expectancy and geriatric evaluation.
SIOG recommendations for standard RT in the Elderly: Prostate Cancer

Future Directions

• Systematic geriatric assessment in (i) the decision tree of treatment policies and (ii) patient selection for brachytherapy

• Trials to assess the role of radiotherapy versus hormone therapy, watchful waiting and surgery

• Hypofractionated EBRT- and IMRT-specific studies for elderly patients
SIOG recommendations for standard RT in the Elderly: Breast Cancer

- Fit older patients are candidates for postoperative WBRT after BCS for invasive cancer and for higher-risk DCIS.

- WBRT with a boost to the site of excision is appropriate for all older patients with invasive breast cancer. There is no specific subgroup from whom WBRT can be systematically omitted.

- Patients \( \geq 50 \) years of age are candidates for shortened treatment schedules when they do not need any lymph node irradiation.

- Partial breast irradiation should be considered investigational as there is insufficient evidence to support it in the elderly.
SIOG recommendations for standard RT in the Elderly: Breast Cancer

- Post-mastectomy irradiation should be considered for older patients with pT3-4 tumours or those with ≥ 4 axillary nodes.

- Axillary irradiation is recommended for macrometastases on sentinel node biopsy or axillary node sampling.

- 3D CT-based planning is advised to minimise cardiac and lung irradiation, as are alternative techniques such as treatment in the prone or lateral position.
SIOG recommendations for standard RT in the Elderly: Breast Cancer

Future Directions

• Identification of ‘low-risk’ population for omission of radiotherapy after breast-conserving surgery

• Role of partial breast irradiation

• Alternative new techniques which reduce morbidity
• Conformal short course RT with or without concomitant temozolomide can be advised for elderly patients with malignant glioma. For elderly patients whose tumour shows MGMT methylation it is reasonable to treat initially with temozolomide alone reserving RT for patients with progressive disease.

• For elderly patients with limited brain metastases, focal stereotactic radiation (radiosurgery) can be recommended due to similar results in terms of survival and less neurotoxicity than whole brain radiotherapy.
Future Directions

- Improved imaging (co-registration using MRI scan with sequences including GD-T1 and diffusion, and PET scan with methionine) of brain metastases to exclude multiple metastases and allow treatment with focal radiotherapy
  - Identification of subsets of glioblastomas to be treated with temozolomide alone (positive MGMT methylation or large radiation volume) or radiotherapy alone (negative MGMT methylation)
SIOG recommendations for standard RT in the Elderly: Lung Cancer

- While surgery remains the standard of care in early-stage NSCLC in the elderly, SBRT is a reasonable option in early-stage NSCLC when surgery is contraindicated.

- For inoperable loco-regionally advanced NSCLC, concomitant chemoradiation is appropriate in fit elderly patients.

- For operable loco-regionally advanced NSCLC, no elderly-specific recommendations can be made concerning post-operative indications, where decisions should be individualised.

- In limited-disease SCLC, chemoradiation in the fit elderly is appropriate, with adapted regimens where necessary.
SIOG recommendations for standard RT in the Elderly: Lung Cancer

Future Directions

• Prospective studies comparing SBRT to surgery (both standard and limited, e.g. wedge resection) in the elderly

• For both locoregionally advanced NSCLC and limited-disease SCLC, investigation of concomitant treatment strategies

• Incorporating newer chemotherapy and targeted agents, potentially less toxic than current cisplatin-based standards

• Refine gating techniques and investigate adaptive RT to further limit the toxicity of curative thoracic RT

• Role of supportive care
For early-stage Hodgkin's lymphoma (HD), involved-field radiotherapy (IFRT) after short-course chemotherapy is appropriate for elderly patients.

For elderly patients with more advanced HD and stage 1-2 non-Hodgkin’s lymphoma, IFRT is an option in cases of symptomatic recurrence and in all patients with low-grade lymphoma.

In some cases of localised disease, involved-node radiotherapy (INRT) can be considered, using new techniques as IMRT or 3D to decrease the toxicity.
SIOG recommendations for standard RT in the Elderly: Lymphoma

Future Directions

- PET-CT-based conformal radiotherapy in patients with comorbidities

- Duration of effect of low-dose radiotherapy (2 Gy × 2) for low-grade lymphoma
SIOG recommendations for standard RT in the Elderly: Endometrial Cancer

- **Low-risk patients:** no adjuvant treatment is required.

- **High-intermediate risk patients:** VB alone is the adjuvant treatment of choice.

- **High-risk patients:** no optimal treatment is defined for the elderly. EBRT ± VB is a reasonable option for this group. Combined modality treatment is commonly used for extra-uterine disease.
Future Directions

• In patients unsuitable for brachytherapy because of technical or medical reasons, can IMRT be considered in terms of a daily adaptive modality image-guided IMRT?
SIOG recommendations for standard RT in the Elderly: Pancreatic Cancer

- Patients who cannot undergo resection can safely undergo SBRT with the expectation of local control at low toxicity.

- The role of adjuvant radiation is unclear, with available data in patients ≥75 showing a 2 year but not 5 year survival benefit, so patient selection is key.

**Future Directions**

- Integration of novel systemic and potentially radio-sensitising targeted agents along with SBRT to improve outcomes

- Clarification of the benefit of adjuvant RT in the elderly node positive and node negative patient populations compared with chemotherapy alone
SIOG recommendations for standard RT in the Elderly: Oesophageal Cancer

• Early data suggests oesophageal cancer IMRT may have better outcomes compared with 3DCRT.

• Consider IMRT for elderly patients, possibly with a tumour dose escalation if medically inoperable.

Future Directions

• Prospective validation of IMRT for patients with locally advanced disease to determine potential superiority of outcomes compared with 3D CRT

• Investigation of dose escalation strategies as definitive therapy in elderly patients with contraindications to resection
SIOG recommendations for standard RT in the Elderly: Rectal Cancer

- Elderly patients with locally advanced rectal cancer can safely receive preoperative long-course chemoradiation with 5-fluorouracil chemotherapy or a one-week short course of pelvic radiation alone.

- For elderly patients with early rectal cancer who are medically inoperable, endorectal contact X-ray treatment offers the potential for local control without significant toxicity.

- Tailored strategies for those elderly patients who receive preoperative treatment with a complete clinical response, such as surveillance or transanal endoscopic microsurgery (TEMS), may be appropriate if there are contraindications to radical surgery, which remains the standard of care.
Colorectal cancer oligometastases to the lung and liver can be treated with stereotactic ablative radiotherapy in elderly patients not eligible for surgery, with minimal morbidity and a high likelihood of local control.
SIOG recommendations for standard RT in the Elderly: Rectal Cancer

Future Directions

- Identification of a pre-treatment molecular signature to indicate those patients likely to be complete responders

- Identification of additional agents that can be given concurrently with radiation using advanced technologies to improve the response rate while not increasing morbidity

- Identification of subsets of patients who are candidates for radiation to a smaller volume in order to avoid the morbidity of whole pelvic RT
SIOG recommendations for standard RT in the Elderly: Head and Neck

- Radical RT using IMRT or other highly conformal techniques to reduce acute and late toxicity is appropriate in elderly patients without severe comorbidities.

- Aggressive combined modality treatment is appropriate where comorbidities permit.
SIOG recommendations for standard RT in the Elderly: Head and Neck

**Future Directions**

- Further refinement of IMRT organ-sparing techniques, with prospective studies comparing novel strategies (e.g. carotid-sparing IMRT) and standard RT

- Investigation of other potential concomitant targeted therapies with less toxicity than cisplatin-based regimens and potentially better tolerance than cetuximab
Big Picture Concepts

As a non-invasive local therapy, RT can be delivered ‘easily’ to elderly patients. We can vary the dose, no. of fractions, size of the field, complexity of technology to fit the particular situation. Question is what are we looking to achieve? (And at what cost?)

- Trial Design and Generalizability
- Chronological Age, Co-morbidities, Functional Status
- Patient Factors, Disease Factors, Treatment Factors
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Future Directions and Conclusions

• Geriatric Oncology is here to stay

• Trials pertaining to this population are clearly needed

• Proper Geriatric Assessment is necessary to identify prognostic/predictive factors

• For now, awareness of various RT modalities/approaches plus knowledge of available evidence is needed to guide individualized management
COMPREHENSIVE GERIATRIC ASSESSMENT

Functional status

- Activities of Daily Living (ADL) - Eating, dressing, continence, grooming, transferring, using the bathroom
- Instrumental Activities of Daily Living (IADL) - Using transportation, managing money, taking medications, shopping, preparing meals, doing laundry, doing housework, using the telephone
- Performance status
- Falls
  - In patients who have experienced a fall in the last 6 months or if the patient is “afraid of falling,” consider the following evaluations:
  - Assessment of gait using Timed Up and Go (TUG) test: See SAO-D
  - PT or OT Evaluation
  - Checking and replacing Vitamin D levels
  - Referral to geriatrics or primary care physician
- Gait speed

Socioeconomic issues: See SAO-2

Psychosocial distress: See NCCN Guidelines for Distress Management

Comorbidities

- May affect treatment decisions in 5 ways:
  - Comorbidity may modify cancer behavior.
  - Cancer treatment may interact with comorbidity to impact functional status or worsen comorbidity. This includes any drug-drug interactions.
  - Cancer treatment may be too risky because of the type and severity of comorbidity.
  - Comorbidity may influence life expectancy (independent of the cancer).
  - Comorbidity may affect treatment outcome.
COMPREHENSIVE GERIATRIC ASSESSMENT

Cognitive function (See Assessment of Cognitive Function SAO-E)
- Dementia
  - Mini-Mental State Examination (MMSE)²,³
  - Montreal Cognitive Assessment (MoCA)⁴ (http://www.mocatest.org/)
- Depression
  - Geriatric Depression Scale (GDS)⁵,⁶
  - See NCCN Guidelines for Distress Management
- Delirium
  - Confusion Assessment Method and/or Memorial Delirium Assessment Scale⁷,⁸
  - See NCCN Guidelines for Palliative Care and NCCN Guidelines for Distress Management

Polypharmacy
- Medication review (prescription and over-the-counter medications, vitamins, and supplements) for duplication and appropriate use should be performed at every visit and evaluated for potentially inappropriate medication use.
  - Medication Appropriateness Index⁹
  - Beers Criteria¹⁰
  - STOPP/START Criteria¹¹,¹²
- Review drug interactions and drug-supplement interactions¹³
  - http://medicine.iupui.edu/clinpharm/ddis/
- Carefully review indications, duration of therapy, and dosage when using these medications or classes of medications¹⁴,¹⁵
  - Benzodiazepines
  - Anticholinergics
  - Antipsychotics
  - Opioids
  - Corticosteroids
  - Antihistamines
  - Oxybutynin
  - Sleep medications
  - Neuroleptics
  - Antidepressants
  - Anticonvulsants
  - Class 1A antiarrhythmics

- Evaluate adherence to therapy (See Assessment of Adherence SAO-F)

Nutritional status
- Body mass index
- Weight loss
- Nutritional deficiency - Mini Nutritional Assessment (MNA)¹⁶,¹⁷

See References (SAO-C 3 of 3)