



Position Paper

Radiopharmaceuticals in the elderly cancer patient: Practical considerations, with a focus on prostate cancer therapy

A position paper from the International Society of Geriatric Oncology Task Force



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Abstract Molecular imaging using radiopharmaceuticals has a clear role in visualising the presence and extent of tumour at diagnosis and monitoring response to therapy. Such imaging provides prognostic and predictive information relevant to management, e.g. by quantifying active tumour mass using positron emission tomography/computed tomography (PET/CT). As these techniques require only pharmacologically inactive doses, age and potential frailty are generally not important. However, this may be different for therapy involving radionuclides because the radiation can impact normal bodily function (e.g. myelosuppression). Since the introduction of Iodine-131 as a targeted therapy in thyroid cancer, several radiopharmaceuticals have been widely used. These include antibodies and peptides targeting specific epitopes on cancer cells. Among therapeutic bone seeking agents, radium-223 (²²³Ra) stands out as it results in survival gains in patients with castration-resistant prostate cancer and symptomatic bone metastases. The therapeutic use of radiopharmaceuticals in elderly cancer patients specifically has received little attention. In elderly prostate cancer patients, there may

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be advantages in radionuclides' ease of use and relative lack of toxicity compared with cytotoxic and cytostatic drugs. When using radionuclide therapies, close coordination between oncology and nuclear medicine is needed to ensure safe and effective use. Bone marrow reserve has to be considered. As most radiopharmaceuticals are cleared renally, dose adjustment may be required in the elderly. However, compared with younger patients there is less, if any, concern about adverse long-term radiation effects such as radiation-induced second cancers. Issues regarding the safety of medical staff, care givers and the wider environment can be managed by current precautions.

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1. Introduction

Diagnostic radiopharmaceuticals are generally pharmacologically inactive and given only in relatively small doses needed for imaging. Such agents are considered to have no measurable pharmacodynamic impact [1]. For these reasons, there is little concern about specific toxicity problems arising with age, although the practicalities of imaging elderly patients need to be considered. In contrast, with therapeutic radiopharmaceuticals, the desired clinical benefit arises from the effects of radiation on the tumour, and courses of treatment may involve frequent administration. In this context, both age-related changes in tissues, such as bone marrow, and questions of altered drug clearance arise.

A Task Force of the International Society of Geriatric Oncology (SIOG) considered practical recommendations on the use of radiopharmaceuticals, both diagnostic and therapeutic, in elderly cancer patients. This increasingly important issue has not previously been reviewed from the perspective of elderly patients. Such a perspective is important because physiological reserves typically decline with age; many elderly patients have significant comorbidities; and there is increased risk of interactions with drugs taken for concomitant disease [2,3].

Systemically administered therapeutic radiopharmaceuticals are used in thyroid cancer (an area in which there is more than 50^o years of experience), in neuroendocrine tumours, in non-Hodgkin lymphoma and in myeloproliferative diseases. However, these tumours are relatively infrequent, even in the elderly.

The most common tumours (lung, colorectal, breast and prostate), show a steeply rising incidence and mortality with increasing age (Fig. 1) [4]. Among these four tumours, the risk of skeletal involvement is high in three: in advanced stages of the disease, bone metastases are present in 47–85% of breast cancer patients, 32–60% of those with lung cancer, and 33–85% of prostate cancer patients [5]. Given the recent increased interest in radionuclides in patients with bone metastases from castration-resistant prostate cancer (CRPC), and as more than 90% of them have skeletal metastases

[6], discussion of the therapeutic use of radiopharmaceuticals focussed on this area.

The general principles underlying radionuclide use in the elderly are likely to be similar to those in younger patients. However, elderly patients have been under-represented in clinical trials, despite the fact that the majority of cancers—and hence of treatment—is in precisely these patients. Hence, as in most areas of oncology, specific data on the efficacy and toxicity of radionuclides in these populations are limited.

Task Force members conducted literature searches in their areas of expertise. We make no attempt to formally assign levels of evidence to recommendations. They should be considered those of an expert group and as the basis for further discussion. The recommendation that more elderly patients should be included in trials is an obvious starting point.

2. Age and frailty: general considerations

While chronological ageing is uniform and relentless, biological ageing is not. The main relevant factors are: (1) functional losses, including those relating to cognition; (2) the effects of declining physiological reserves on resistance to toxicity and on drug handling; and (3) the implications of comorbidities and associated polypharmacy.

The broad concept of frailty, defined as vulnerability in the face of a stressor, is of interest to clinicians assessing the likely side-effects of therapy [7]. Functional status and the presence of comorbidities are the most readily available guides to patients who are especially vulnerable to adverse effects of treatment.

Means of assessing the overall fitness of elderly patients and the likely toxicity of chemotherapy have been developed [2,8,9]. Although they have not been assessed in the context of radiopharmaceuticals, such tools may help predict any toxicity in elderly patients.

In the setting of prostate cancer specifically, a recent International Society of Geriatric Oncology (SIOG) Task Force [3] has advocated initial screening for cognitive impairment, to establish patient competence in making decisions, followed by brief evaluation of health status using the validated G8 screening tool. Abnormal

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