Radiation therapy and radioisotopes for bone metastases: what is their real benefit?

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Bone metastases are a frequent complication of most malignancies. For example about 80–100% of patients with prostate cancer will suffer from metastatic bone disease, which may significantly impair quality of life. Besides being affected by pain, complications like pathological fractures and spinal cord compression may lead to clinical deterioration, to the need for drug treatment, to in-patient care or to bedridden patients. Furthermore, as shown for prostate cancer, the presence and progression of bone metastases is often connected to an impaired prognosis of the underlying malignant disease.

For decades, besides treatment with painkillers and bisphosphonates, percutaneous irradiation as well as radionuclide therapy [1] has been of benefit for the palliation of pain and prophylaxis of complications. Multiple dose and fractionation regimens have been recommended for percutaneous radiotherapy reaching from one-fraction regimens to treatments of several weeks [2], the choice depending on the preference of the treating physician, the predominant clinical problem and the oncological situation of the patient. Several systematic reviews have shown that all these regimens lead to a significant reduction in bone pain, while in certain clinical situations (e.g. impending pathological fractures or metastatic cord compression), regimens with multiple fractions may be preferred to single-fraction treatment [2]. While there are no clear recommendations on the delineation of target volumes for palliative radiotherapy of bone metastases, there are some reports relating local failure to dose distribution and planning technique. In recent years, patients in an oligometastatic situation have been treated with high-dose stereotactic radiotherapy leading to excellent local results [3]. However, most percutaneous radiotherapy treatments for bone metastases are still given in merely palliative intent, being applied after simple and pragmatic treatment planning procedures.

For radionuclide therapy, various radiopharmaceutic drugs like [^{89}Sr]-Strontium-Chloride, [^{153}Sm]-Samarium-Lexidronam and [^{186}Re]-Rhenium-HEDP have been shown to lead to beneficial clinical results in terms of well-documented palliative effects with minimal toxicity [4–6]. In controlled clinical trials, the superiority of radionuclide treatment versus placebo, "cold" nuclides, percutaneous radiotherapy alone [7] and versus bisphosphonate treatment [8] has been demonstrated. Although the aim of radionuclide treatment is palliation, it may also lead to a reduction in number and size of bone metastases and may reduce the need for further treatment for bone metastases further along the course of the malignant disease. Beyond this, for some tumours, an improvement in prognosis by radionuclide treatment for bone metastases has been shown [9].

Recent developments include the combination of radionuclide treatment with chemotherapy [10–12], presently being investigated in prospective clinical multicentre trials, and the use of alpha particles (e.g., [^{223}Ra]-Radium), possibly also leading to a survival benefit in patients with bone metastases from prostate cancer [9].

A sequential combination of percutaneous irradiation and radionuclide therapy may be given rather frequently in the clinical reality of for example thyroid cancer and prostate cancer. However, clinical trials with systematic combination of both treatments are rare. One Canadian study [7] has shown a decrease in the need for further radiotherapy in patients who were given both treatments vs. those who received percutaneous radiation only. The same study group has demonstrated a beneficial socio-economic effect of this treatment combination. However, further studies, e.g. including modern radiopharmaceuticals and modern techniques for percutaneous irradiation, are warranted.

Overall, percutaneous irradiation and radionuclide therapy have both developed to modern and low-toxicity treatment options in metastatic bone disease. Beyond this, survival benefits in selected patient populations by advanced combinations of these modalities

with each other or further treatments may be reached in the future.

Conflict of interest statement

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