
Preface

Skeletal metastases affect more than 80% of men with metastatic prostate cancer, and they are the main cause for patients' poor quality of life, morbidity, and mortality. In the recent years, there was a tremendous improvement in the options of treatment for patients with metastatic prostate cancer. New hormonal, cytotoxic, immunotherapeutic drugs and new therapeutic radiation-based strategies have been developed. These approaches achieved very important results also in terms of overall survival and appear to be suitable for a large number of patients with metastatic prostate cancer, either those affected by hormone-naïve prostate cancer (HNPC) or those affected by castration-resistant prostate cancer (CRPC). One could say that while in the past the majority of patients, especially those affected by CRPC, were candidate only to best supportive care, at present most of them can afford upon different treatment choices able to impact favorably both with their life expectancy and their quality of life as well as upon novel therapeutic options and new combination strategies which promise to further improve patient outcomes.

In view of the increasing interest and number of scientific contributions in this area, we have conceived the idea to invite a number of distinguished colleagues to summarize the state of the art and to examine the new perspectives from their different points of view on the most important topics related to bone metastases in prostate cancer, starting from the physiopathological background of bone metastatization and the biological mechanisms involved in bone remodeling and in skeletal homing of cancer cells, which are the premises to a rational approach to the disease. Markers of these phenomena are described and analyzed in view of their clinical applications in everyday clinical practice. A special focus was given to the putative role of circulating cancer cells, circulating markers of bone metabolism, and markers of prostatic cancer. The metabolic relevance of the mechanisms involved in bone metastatization is also described in the perspective of the technological advancements of metabolic imaging that visualizes bone metastases through new radiopharmaceuticals capable to target bone changes caused by metastasis or directly prostate cancer cells. New modalities of metabolic imaging, such as ^{18}F -fluoride, $^{18}\text{F}/^{11}\text{C}$ -choline, and ^{18}F -FDG positron emission tomography (PET)/computed tomography (CT), are reported, including the most recent experimental tracers like ^{68}Ga -prostate specific membrane antigen (^{68}Ga -PSMA). In the radiological area, the contribution of the multimodality

magnetic resonance imaging (MRI) in improving the accuracy of CT has been critically discussed, also in terms of availability of this technique and relative costs. As a logical consequence of an adequate diagnosis and staging, attention was moved to the available treatment options for patients with prostate cancer bone metastases (hormonal therapy, chemotherapy, chemotherapy associated with hormonal manipulations, bone targeted drugs, surgery, external beam therapy, and radio-metabolic therapy). The evaluation of treatment response in bone metastatic prostate cancer is one of the key points addressed in the textbook due to the limits of currently available tools, namely, radiology and nuclear medicine imaging. The putative advantages of one or more techniques over the others have been specifically analyzed. The putative role in implementing the definition of tumor response at the bone level by the dosage of markers of bone turnover and of prostate-specific antigen (PSA) has been also considered. The performances and limitations of the criteria adopted in the most important clinical trials and which are currently recommended by the Guidelines of the Scientific Societies have also been critically reviewed. A look at other issues that are strictly correlated with the management of the patients affected by bone metastases has been provided. The abovementioned issues include bone pain palliation and prevention of major adverse skeletal events as well as the social and economic impact of bone metastases, which intuitively is not limited to the costs more directly related to patient care. The necessity of addressing this increasingly important health problem through a multidisciplinary team of clinicians able to intercept all the patient needs and to provide an appropriate answer to all of them has also been addressed, with the hope that this model could become standard for the majority of the centers involved in the management of prostate cancer. Our ambition, as editors of this volume, was to provide the readers with a complete but clear-cut information about the most relevant results achieved in the different areas concerning the topic as well as a look at the researches that are still going on and that promise to further change the course of the disease and of its management. Let's hope we have reached the scope, thanks to the efforts of the authors who have accepted to actively provide their contributions and to the editor staff who trusted in this task and whose help and assistance was essential to complete it.

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