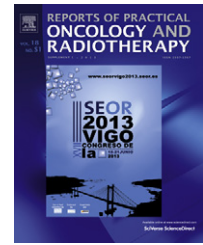


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## Refresher course: Oligometastasis

# The metastatic cascade and patterns of metastasis



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## 1. Introduction

The oligometastatic disease concept was proposed by Hellman and Weichselbaum in 1995 as a third hypothesis of the pathogenesis of cancer.<sup>1</sup>

The classic dilemma between tumors that could be cured with local treatment, surgery and/or radiotherapy because the tumors were partly spread and the metastatic disease mostly could only be treated with systemic palliative treatment, may be completed with a third theory: some tumors and metastatic disease could be treated with local treatment with curative intention. The dissemination of certain tumors would be done in a controlled and limited way that would allow the use of surgery, radiotherapy and other ablative treatments. This approach has been demonstrated in the central nervous system metastases treated with surgery, radiotherapy and radiosurgery, as well as liver and lung metastasis treated with surgery. The same authors participated in a clinical trial with 60 patients with 113 metastases where radiotherapy dose titration was prospectively studied between November 2004 and November 2009.<sup>2</sup> The progression-free survival at two years was 22% and the overall survival at two years was 56.7%. Eleven patients (18.3%) did not progress. The importance of this approach is determined by better selection of patients with more precise techniques, to study the contribution of systemic treatments, and also increase the knowledge of the metastatic process. Current understanding about the complexity of tumor biology can overcome the classical theory of Halsted where the spread was done in an orderly spreading to contiguous regions such as lymph nodes and later to distance.<sup>3</sup> The subsequent theory of Bernard Fisher and colleagues suggesting the need for chemotherapy for most patients to treat cancer of a more systemic than local is also overcome by clinical observations.<sup>4</sup> But since the “seed and soil” Paget’s hypothesis where the metastasis depends on

interaction of the tumor cell and the host microenvironment, the advancement of knowledge does not allow prediction of the behavior of the most tumors.<sup>3</sup>

The main issue is to understand the biology of the oligometastatic phenotype, if it really exists. Just as there are already tests for selecting patients and avoid adjuvant chemotherapy, we have no tools to ascertain the oligometastatic situation.<sup>5</sup> Lussier and colleagues analyzed the expression of microRNAs in lung metastases in patients with less than 5 metastases and curative treated classified according to the percentage of recurrence.<sup>6</sup> The selected microRNAs were able to distinguish between high and low probability of disease recurrence in a series of validation, establishing a molecular hypothesis oligometastatic disease. However, the great heterogeneity of tumors is responsible for the large clinical and molecular variability, forcing us to reevaluate the metastatic cascade. A small proportion of cancer cells, so-called circulating tumor cells acquire properties necessary to invade and grow in distant organs. The molecular characterization of these circulating cells is an innovative approach to predict clinical behavior of tumors.<sup>7</sup>

Apart from the controversy about the various models and theories of the metastatic process, the important thing is to increase our knowledge that will allow us to treat patients with the most effective and less toxic treatments. The complexity of biology will lead us to treat groups of patients based on the disease prognosis and treatment prediction.

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