(172,173,174,175,176,177). When CTCs are measured, the nature and number of these cells represent those freshly released from the primary tumor, as well as those released from site of metastasis. Sites of metastasis can include the bone marrow. To this point, Cen et al. (178) state that, "[c]irculating tumor cells (CTCs) are tumor cells disseminated from primary and metastatic sites and can be isolated from peripheral blood."

Cen et al. (179) disclose another advantage of CTC over biopsies of the primary tumor, namely, the advantage that CTC sampling and analysis is more representative of the types of tumor cells in the patient's body. To this end, Cen et al. state that, "[t]raditional tumor biopsy sampling can only capture part of the tumor and is unable to represent the entire tumor cell population or identify changes that occur over time. Ongoing analysis of CTCs not only has the potential to represent all cells shed from primary pancreatic tumor and each metastatic site."

CTCs have been used in early-stage cancer, as well as in metastatic cancer (late-stage cancer). The following concerns the biology of CTCs in breast cancer. In short, cancerous cells from breast cancer tumors migrate to the bone marrow. The *breast cancer* cells that migrate to the bone and reside in the bone are called "disseminated tumor cells" (180). Once establishing residence in the bone marrow, the breast cancer cells represent "minimal residual disease," and can be detected directly by way of a bone marrow biopsy. When the cells representing minimal residual disease leave the bone marrow, they are called "circulating tumor cells," and can be detected without the need for a bone marrow biopsy.

Riethdorf and Pantel (181) disclose that *breast cancer* cells leave the primary tumor to become CTCs, and that these CTCs migrate to

[172]Toss A, et al. CTC enumeration and characterization: moving towards personalized medicine. Ann. Transl. Med. 2014;2:108 (16 pp.).

[173]Wallwiener M, Riethdorf S, Hartkopf AD, et al. Serial enumeration of circulating tumor cells predicts treatment response and prognosis in metastatic breast cancer: a prospective study in 393 patients. BMC Cancer 2014;14:512 (12 pp.).

[174]Grobe A, Blessman M, Hanken H, et al. Prognostic relevance of circulating tumor cells in blood and disseminated tumor cells in bone marrow of patients with squamous cell carcinoma of the oral cavity. Clin. Cancer Res. 2013;20:425-33.

[175]Broersen LH, et al. Clinical application of circulating tumor cells in breast cancer. Cell Oncol. (Dordr). 2014;37:9–15.

[176]Young R, Pailler E, Billiot F, et al. Circulating tumor cells in lung cancer. Acta Cytol. 2012;56:655–60.

[177]Liandou ES, Markou A. Circulating tumor cells in breast cancer: detection systems, molecular characterization, and future challenges. Clin. Chem. 2011;57:1242–55.

[178]Cen P, et al. Circulating tumor cells in the diagnosis and management of pancreatic cancer. Biochim. Biophys. Acta 2012;1826:350–6.

[179]Cen P, et al. Circulating tumor cells in the diagnosis and management of pancreatic cancer. Biochim. Biophys. Acta 2012;1826:350–6.

[180]Hartkopf AD, Wallwiener M, Hahn M, et al. Simultaneous detection of disseminated and circulating tumor cells in primary breast cancer patients. Cancer Res. Treatment 2012. http://dx.doi.org/10.4143/crt.2014.287.

[181]Riethdorf S, Pantel K. Disseminated tumor cells in bone marrow and circulating tumor cells in blood of breast cancer patients: current state of detection and characterization. Pathobiology 2008;75:140–8.