of TDM over the course of 15 years. The hazard ratio for TDM was HR = 1.52 (P = .006), which indicates a moderate separation between arm A and arm B.

The authors provided an additional, different Kaplan-Meier plot showing the percentage of subjects triggering the endpoint of survival (dying), over the course of 15 years. The hazard ratio for overall survival was only HR = 1.18 (P = .12), indicating almost no separation between the study arms.

The investigators were pleased with the improvement in TDM found in arm A, writing that the delayed time for 40% of patients to develop metastasis by 8 years with the addition of just 4 months of neoadjuvant ADT with EBRT is "remarkable" (19). The term ADT refers to androgen deprivation therapy, while EBRT refers to radiotherapy.

Thus, the Roach study shows the utility of using the endpoint of TDM, in that a clear separation between study arms may be reached prior to separation with the endpoint of overall survival. Also, the utility of TDM may be that study arms using the endpoint of TDM may be clearly separated, but that clear separation between study arms may never be reached with the endpoint of overall survival.

IV. USE OF A GENE ARRAY AS A PROGNOSTIC FACTOR FOR BREAST CANCER PATIENTS, USING THE ENDPOINT OF TIME TO DISTANT METASTASIS – THE LOI STUDY

A recurring theme in this textbook is the use of biomarkers in clinical trials. In one of the sets of analyses from the following clinical trial, all subjects received the same drug (tamoxifen). Expression of a group of genes (97 genes) was measured in all tumor samples. The authors configured the gene expression data in terms of a score, which they named, "Gene expression Grade Index" (GGI). In detail, the expression of the 97 genes was subjected to an algorithm which, for any given patient, resulted in a high GGI score or a low GGI score. The goal of the study was to determine if the GGI score (high or low) could be correlated with the endpoint of time to distant metastasis (TDM). In a study of breast cancer, Loi et al. (20) analyzed biopsies from 417 breast cancer patients.

Gene expression from each tumor biopsy was measured using a microarray sensitive to 97 genes. These 97 genes are identified by Sotirou et al. (21). As a matter of introduction to the genes included in this set, it was found that the top overexpressed

[19] Roach M, Bae K, Speight J, et al. Short-term neoadjuvant androgen deprivation therapy and external-beam radiotherapy for locally advanced prostate cancer: long-term results of RTOG 8610. *J Clin Oncol*. 2008;26:585–591.

[20] Loi S, Haibe-Kains B, Desmedt C, et al. Definition of clinically distinct molecular subtypes in estrogen receptor-positive breast carcinomas through genomic grade. *J Clin Oncol*. 2007;25:1239–1246.

[21] Sotiriou C, Wirapati P, Loi S, et al. Gene expression profiling in breast cancer: understanding the molecular basis of histologic grade to improve prognosis. *J Natl Cancer Inst*. 2006;98:262–272.