

## Targeted Therapy in the Macro Mode

Two exciting trends are evident in oncology right now. First, we have a plethora of new drugs with proven clinical benefit: witness the dramatic changes in managing colorectal cancer. Second, many of the anti-neoplastic agents can target specific steps in genetic pathways, as we move ever closer to the ideal “silver bullet.”

These targeted advances at the micro or cellular level are not without consequences, however. Health economists have raised warning flares that the greater expenditures required to support more aggressive and complex treatment regimens may eventually exceed the system’s capacity to sustain these breakthroughs.

On a macro level, that we are exploring targeted approaches that may actually limit treatments while improving effectiveness and perhaps saving valuable health care dollars is intriguing. The goal of good oncology management has always been to identify patients who need treatment and avoid treating those who will not benefit, avoiding potentially debilitating side-effects. For patients who need or would benefit from treatment, the goal has been to find the least aggressive treatment that will yield optimal outcomes.

The problem has been, of course, that we had relatively few tools with which to differentiate between these important patient subsets and little data with which to match treatment aggressiveness to disease severity. In this issue, the articles by McCormick on partial breast irradiation and Jeffrey et al. on genetic profiling of breast cancers show, on the macro level, the feasibility of more targeted therapy that may, in some instances, lead to less- rather than more-intensive treatment.

Whole breast radiation has been a major part of the standard adjuvant management of early breast cancer as delineated in the NCCN Breast Cancer guideline (in this issue). Although recent data may allow skipping this modality in low-risk groups<sup>1</sup> (age > 70, tumor < 2 cm, estrogen receptor positive, taking tamoxifen), for the most part radiation is a blanket recommendation for all women undergoing breast-conserving surgery. The introduction of partial breast irradiation has the potential to open up a new avenue in targeting treatments for certain groups. Despite its proven efficacy in preventing local recurrences, variability in the use of whole breast radiation therapy has been well documented.<sup>2</sup> A major barrier has been distance from a radiation facility preventing some women from receiving the currently recommended 5-6 week courses of therapy.<sup>3</sup> Similarly, the documentation that low-income women may not receive radiation compared to other groups may reflect the difficulty of dealing with protracted treatments.<sup>4</sup> The development of a new shortened therapeutic approach may allow certain appropriate groups with small tumors and clean margins to receive this more compact therapy.

The ultimate pay-off of targeted therapy on the macro level may rest with the application of gene array profiles as prognostic and predictive markers to ascertain which patients may require treatment and perhaps more importantly which will respond to treatment. Spurred on by the major advances in gene identification technology, the development of accurate markers presages major advances in the ability to direct therapies to the right patients.<sup>5</sup>

The future, then, appears optimistic: not only will we have treatments that target tumors with a fine beam and spares normal tissues, we will also be able to target patients most likely to benefit and spare those who would suffer the



### By Rodger J. Winn, MD

Rodger J. Winn is the Editor-in-Chief of *JNCCN*. He is Clinical Consultant at the National Quality Forum, and his past positions include Associate Professor of Clinical Medicine at the University of Texas M. D. Anderson Cancer Center. Dr. Winn received his medical degree from Jefferson Medical College of Philadelphia. His post-graduate training includes an internship and residency at Jefferson Medical College, and he also completed a medical oncology fellowship at Memorial Sloan-Kettering Cancer Center in New York. He is board certified in internal medicine and holds subspecialty certification in oncology.

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harms but experience none of the gains of our interventions. As always, our mantra applies: only well-designed trials can bring these changes about.

## References

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