



Surgery and Radiotherapy for Breast Cancer: A Look at the Studies

In December of 2005, the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) published the combined results of 78 clinical trials evaluating radiation therapy and surgery in breast cancer patients.

The group has published updates of this data every 5 years, and this publication represents 15 years of follow-up. The paper is jam-packed with statistical data and graphs that present some impressive results, but make it difficult for a patient to apply the results to their own situation. OncoLink has asked Dr. Lawrence J. Solin, Professor of Radiation Oncology at the University of Pennsylvania and long-time friend of OncoLink, to help us make sense of this new data.

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: Dr. Solin, thank you for speaking with us today about this exciting new data. The type of study used by the EBCTCG to examine this data is called a meta-analysis; can you explain what that is?

Dr. Solin: Meta-analysis is simply a mathematical way of analyzing data from existing randomized clinical trials. In a meta-analysis, all known randomized trials are combined or added together, allowing for larger numbers of patients to be evaluated. This gives us the ability to look at randomized trials in a different way, one that often gives important and novel information.

In the recently published meta-analysis (or Overview) from the Early Breast Cancer Trialists' Collaborative Group (EBCTCG), all randomized clinical trials that evaluated local treatment (radiation treatment or surgery) were included. This meta-analysis led to important and new findings demonstrating the importance of local-regional treatment to minimize local-regional recurrence as well as to improve survival.

We should take a minute to explain that local-regional treatment is therapy for the breast and the lymph nodes around the breast. In the case of breast conserving surgery or lumpectomy, "local" refers to the breast. In the case of a mastectomy, "local" refers to the mastectomy scar and surrounding tissues in the chest wall. "Regional" refers to the lymph nodes in the region surrounding the breast. In most of these studies, women only received regional treatment for lymph node-positive disease.

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: The studies that were included examined mastectomy, breast conserving surgery (or lumpectomy), both with and without radiation. Most patients also underwent axillary lymph node dissection, as sentinel node technology was not being practiced at that time. In order to have 15 years of follow-up on this number of patients, some patients would have had to begin treatment as far back as the 1970's, correct? How have radiation therapy treatments changed since then?

Dr. Solin: Radiation treatment for breast cancer has undergone dramatic changes over the last 10 -20 years. Part of this relates to improving technology, and part to a better understanding of the biology of breast cancer. Newer radiation treatment machines allow for better planning and targeting of the areas at risk that need to be treated, while reducing or even eliminating the radiation dose delivered to normal tissues, such as the heart and lung. Also, we now have a better understanding of how to integrate radiation with other treatments, such as surgery and chemotherapy. This allows contemporary radiation treatment programs to be designed for maximal control and cure rates, often with a low risk of complications.

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: Does this continuing evolution of radiation therapy make it difficult to apply these results to today's treatments?

Dr. Solin: Partly yes, and partly no. One of the important lessons from the current Overview is that radiation complications, although fortunately very uncommon, can be a late occurrence. This analysis included many different radiation therapy techniques, allowing us to see which techniques led to higher complication rates. Understanding the late events associated with various techniques guides us on how to design current radiation treatment plans to minimize the risk of these late

complications. Also, this Overview shows that breast cancer patients need to be followed for long periods of time after treatment in order to fully understand the potential late effects of any given treatment. We hope that the lessons learned from this Overview will lead to fewer long term complications.

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: Let's talk about the results. What are the numbers, and what do women need to learn from these studies to help them understand and make treatment decisions?

Dr Solin: There are a number of important lessons here. First and foremost, local-regional treatment and local-regional control are important. Although we often hear about the wonderful and promising results from systemic therapies and new biologically targeted agents, we should always remember that maximizing local-regional treatment continues to be a key element for maximizing the chances for cure in our breast cancer patients. The results here were impressive. One death from breast cancer is avoided for every four local-regional recurrences (those in the treated breast, chest wall, or surrounding lymph nodes) that were prevented through the use of optimal local-regional treatment.

Another important finding is that the importance of local-regional treatment holds true for patients undergoing either breast conservation or mastectomy. As I mentioned, the Overview has also given us important information on how to reduce the late risks of radiation complications. Finally, long-term follow-up after any form of breast cancer treatment is important to fully understand its effects. In the early years of this analysis, the improved survival outcomes were not as obvious; it is only many years later that we truly see the benefits of this therapy in terms of decreased recurrence and increased survival.

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: Some women are concerned about the long term effects of radiation therapy, such as secondary cancers (lung and breast) and heart disease. What have these studies taught us in regards to these concerns?

Dr. Solin: This is an important question. As the cure rate for breast cancer after treatment rises, minimizing the potential for late complications, even uncommon ones, becomes increasingly important. The current Overview has given us important information about certain technical radiation treatment factors. Changes in these techniques based on this Overview are expected to result in lower rates of complications. Lastly, one very important finding was that the benefit from adding radiation treatment and maximizing local-regional control was substantially greater than the risk of late complications for these women. In short, the benefit of radiation treatment was much greater than the risk of complications from treatment.

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: Will the EBCTCG continue to follow these women? And can we expect to see this type of long-term follow up in some of the more recent techniques, such as sentinel lymph node biopsy, which were not in used in these trials?

Dr. Solin: I certainly hope so. There are any number of new breast cancer treatment approaches that should be studied in the same way. Sentinel lymph node biopsy is one new surgical approach, and there are also a number of valuable, new systemic therapies, such as herceptin and aromatase inhibitors, that deserve long term follow-up.

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: What do you see as the take-home message for women who are facing decisions regarding breast cancer treatment?

Dr. Solin: The take-home message here is simple. For patients with breast cancer, local-regional treatment and local-regional control are important!

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