Hypofractionated Radiotherapy For Breast Cancer

A recent study led by Penn's Dr. Justin Bekelman has received wide news coverage, renewing discussions about the number of radiation treatments needed for some women with breast cancer. In this article, we will review the role of radiotherapy in early stage breast cancer, discuss the evidence for hypofractionated treatment, and examine the study from Bekelman and colleagues.

What is breast-conserving surgery?

Many women with early stage breast cancer will be treated with breast-conserving surgery (BCS). During BCS, a surgeon cuts out the tumor while leaving the rest of the breast intact. This is different than a mastectomy, where the entire breast is removed.

What are the benefits of radiotherapy after BCS?

Although BCS cuts out the visible tumor, it is possible for microscopic cancer cells to be left behind. Radiotherapy—a cancer treatment using high-energy x-rays—can be given after BCS to kill any tumor cells remaining in the breast. The goals of radiotherapy are to prevent the cancer from coming back and, ultimately, to improve survival.

How much of an impact does radiotherapy have? Consider a woman with early stage breast cancer who undergoes BCS. If no radiotherapy is given, on average the chance of the cancer coming back is 35% and the chance of dying from the cancer is 17% within 10 years. If radiotherapy is given, on average the chance of the cancer coming back is 19% and the chance of dying from the cancer is 14% within 10 years. These numbers can be viewed another way. Suppose we treat 100 women with radiotherapy after BCS. The treatment will prevent the cancer from coming back for 18 of those women and it will save 3 of their lives.

What is fractionation?

As we discussed before, radiotherapy uses high-energy x-rays to kill tumor cells. A certain total dose of radiation must be delivered for the treatment to be effective. However, it would be too toxic to give this entire dose in a single day. Radiotherapy is therefore fractionated, or split up into many smaller daily doses, which add up to the total necessary dose. Standard whole-breast irradiation (WBI) delivers the total dose over 5-7 weeks. Hypofractionated WBI delivers the total dose over 3 weeks. In other words, standard fractionation consists of more days with a smaller dose given each day, while hypofractionation consists of fewer days with a slightly larger dose given each day.

What are the benefits of hypofractionated WBI?

Because there are fewer days of treatment, hypofractionated WBI is more convenient for patients. It also uses less healthcare resources (i.e. the radiation machine is available to treat other patients). Finally, hypofractionated WBI is not as expensive as standard WBI.

Is hypofractionated radiotherapy safe and effective?

Multiple randomized trials comparing hypofractionated WBI to standard WBI have shown no differences between the two approaches over 10 years of follow-up. Let's look at two of these studies in more detail:

The Standardisation of Breast Radiotherapy (START-B) trial was performed in the United Kingdom. This study randomized 2,215 women to either standard WBI given in 5 weeks or hypofractionated WBI given in 3 weeks. The hypofractionated WBI was shown to be as effective as standard WBI (just as likely to prevent cancer from coming back) and as safe as standard WBI.
(not any more likely to cause rib fractures, lung problems, heart problems, or cosmetic changes to the breast) over 10 years of follow-up.

The Ontario Clinical Oncology Group trial was performed in Canada. This study randomized 1,234 women to either standard WBI given in 5 weeks or hypofractionated WBI given in 3 weeks. Similar to the START-B results, the Ontario study showed that hypofractionated WBI was as effective as standard WBI (no differences in cancer coming back and no differences in survival) and as safe as standard WBI (no differences in skin side effects or cosmetic breast outcomes) with 10 years of follow-up.

Why are some women not treated with hypofractionated WBI?

One concern about hypofractionated WBI is long-term side effects and cosmetic changes to the breast (shrinkage, fibrosis, prominent blood vessels). Remember that the trials discussed above did not show any differences in side effects or cosmetic breast changes between hypofractionated WBI or standard WBI over 10 years of follow-up. However, it is possible that after 15 or 20 years there might be a difference. Another important point is that the studies discussed above enrolled a certain type of patient. The majority of women on those trials were over age 50, had tumors smaller than 5 centimeters, had no cancer in their lymph nodes, and did not receive chemotherapy. Therefore, for women without these characteristics the evidence for hypofractionated WBI is not as strong.

What questions did the Bekelman study ask?

The Bekelman study asked two main questions. First, what percentage of women are receiving hypofractionated WBI versus standard WBI? Second, what is the cost of hypofractionated WBI compared to standard WBI?

Who were the patients in the Bekelman study?

The authors searched an insurance database containing records of 7.4% of all US women from 2008-2013. They found patients who had breast cancer treated with BCS followed by WBI. Among these patients, the authors then selected those who were older than age 50, had no cancer in the lymph nodes, and had not received chemotherapy. This group of patients was most similar to those women who enrolled in the randomized studies discussed earlier—the studies showing hypofractionated WBI was just as safe and just as effective as standard WBI over 10 years of follow-up.

What percentage of these women received hypofractionated WBI in the Bekelman study?

The study found that use of hypofractionated WBI for these women has increased over time. In 2008, 10.6% of these patients received hypofractionated WBI. This number rose to 34.5% in 2013. The remainder of the women received standard WBI.

What was the cost of hypofractionated and standard WBI in the Bekelman study?

The average total healthcare costs within 1 year of breast cancer diagnosis were $28,747 for women treated with hypofractionated WBI and $31,641 for women treated with standard WBI. The average radiotherapy-specific costs were $12,622 for women treated with hypofractionated WBI and $16,961 for women treated with standard WBI.

What were the authors’ conclusions?

The authors quantified the average healthcare savings associated with hypofractionated WBI ($2,894). They also concluded that use of hypofractionated WBI is increasing over time. However, only about 1/3 of women eligible for hypofractionated treatment are currently receiving it—the other 2/3 are getting standard WBI.

How can I use this information?

If you or someone you know is at least 50 years old and had early stage breast cancer removed by breast-conserving surgery, you should speak with your radiation oncologist about different options for WBI. You should review both standard WBI and hypofractionated WBI to determine which treatment is right for you.
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