

**QUESTIONS AND ANSWERS**  
**ABOUT**  
**BREAST CANCER,**  
**BONE METASTASES, &**  
**TREATMENT-RELATED**  
**BONE LOSS**

**A PUBLICATION OF**  
**THE BONE AND CANCER FOUNDATION**



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## The Relationship Between Breast Cancer and Bone Health

### 1. Q: How can breast cancer affect bone health?

**A: Breast cancer can affect bone in two ways:**

- Breast cancer can spread (metastasize) to bone.
- Some breast cancer treatments can cause rapid bone loss.

## The Risk of Breast Cancer Returning and Where

### 2. Q: How often does breast cancer that has been treated return?

**A: The chance of breast cancer returning depends on the type of breast cancer and how it was treated.**

Women with early stage breast cancer who are treated with surgery alone are at risk of having their cancer return, even 15 to 20 years later. The chance of this happening depends on:

- The size of the original tumor.
- Whether the original tumor had spread to local lymph nodes.
- The characteristics of the tissue that made up the tumor.

The risk of breast cancer returning may be lowered by hormonal therapy, chemotherapy, and/or radiation therapy.

### 3. Q: If breast cancer returns, where is it found?

**A: Breast cancer may return to the breast area or spread (metastasize) to other parts of the body.** This happens when tumor cells from the original cancer break off and travel through the blood stream to a new location, where they grow and multiply.

**If breast cancer returns, it often spreads to the bones.** For example, approximately 18 to 20 percent of women diagnosed with early breast cancer will have their cancer return within 10 years of diagnosis. Among these women, 70 percent have cancer that has spread to their bones. Breast cancer can also spread to other organs such as the lungs, liver, or brain.

### 4. Q: What happens when breast cancer spreads to bone?

**A: Over time, the cancer may cause:**

- Changes in the bone.
- Bone pain.
- The bone to break or fracture.

## Decreasing the Chance of Breast Cancer Spreading to Bone

### 5. Q: What can be done to decrease the chance of breast cancer spreading to bone?

**A: When breast cancer is diagnosed, the choice of treatment is made on a case-by-case basis. The following information describes the effect different treatments can have on the risk of breast cancer returning or spreading to bone.**

Hormonal therapy or chemotherapy may decrease the risk of breast cancer spreading to bone. When treating newly diagnosed early stage breast cancer, certain forms of hormonal therapy, chemotherapy, and/or targeted antibody therapies such as trastuzumab (Herceptin®) decrease the risk of breast cancer spreading to other organs – including bone – by 25 to 50 percent. These treatments are usually begun after the breast cancer is removed by surgery. However, in some cases the treatments are given before the surgery takes place.

Radiation given to the breast or chest wall after surgery decreases the risk of breast cancer returning to that area or spreading to other parts of the body.

## Finding Out if Breast Cancer Has Spread to Bone

### 6. Q: How is the spread of breast cancer to bone detected?

**A: When a woman who has had breast cancer reports a new pain that feels like it is in her bones, her doctor will take a careful history and give her a physical exam. The doctor may then order medical tests that give a closer look at the bones. These tests may include:**

- X-ray.
- CAT (Computerized Axial Tomography) scan – also called CT scan.
- Bone scan.
- PET (Positron Emission Tomography) scan.
- MRI (Magnetic Resonance Imaging) scan.

The test(s) selected depends on the woman's symptoms, the bones involved, and what the bones look like on x-ray. For example, a CT scan may be ordered for a problem in an arm or leg. If a bone in the spine (vertebra) is involved, an MRI scan may be used. Bone scans are often done to look at the entire skeleton. The various tests that are used look for:

- Thinning of bone caused by breast cancer cells.
- A scar in the bone that may be caused by:

- a) the breast cancer, or
- b) bone cells filling in thinned bone after the bone has been treated to kill cancer cells.

Sometimes a bone biopsy is needed. A biopsy (removal of a small amount of tissue) of an area of bone that looks abnormal on x-ray may be done to see if breast cancer cells are present. A bone biopsy is often done when other tests do not clearly identify whether breast cancer has spread to the bone.

Finally, the patient's blood may be tested to measure levels of:

- Calcium (an element found in bone).
- Vitamin D (a vitamin that is important for bone health).
- Serum alkaline phosphatase (an enzyme made by bone cells).
- Other compounds that reflect what a tumor is doing to bone.

### **7. Q: Which parts of the skeleton are most likely to be affected by breast cancer?**

**A: The bones most likely to be affected are the ribs, pelvis, and spine; sometimes the arms and legs are affected as well.**

Breast cancer can spread to any part of the skeleton. However, tumor cells most often affect the bones that have the greatest blood supply. These include the ends of the arms and legs (nearest the torso), the pelvis, the ribs, and the spine.

## **Problems Caused by Breast Cancer in Bone**

### **8. Q: What problems are caused by the spread of breast cancer to bone?**

**A: Breast cancer in the bone can cause pain, fractures, pressure on the nerves of the spinal cord, and high levels of calcium in the blood.**

Patients who experience any of the symptoms described below should tell their doctor at once because there are good treatments for each and it is important to start them quickly.

Pain that feels like it is in the bone is the most common symptom that breast cancer has spread to the bone. Such pain may occur with or without a fracture.

Fractures can occur when the hard surface of the bone is weakened by the growth of breast cancer cells. For example:

- Weight-bearing bones such as those in the legs are at highest risk of such fractures. Accordingly, pain in the knee, thigh, or groin when walking may be a symptom of breast cancer that has spread to the bone. Such pain can be a warning that the bone could fracture as the result of very little stress, such as that caused by exercise.

- An arm bone weakened by breast cancer may break from stress, for example, from the force of lifting or carrying a heavy object.
- When breast cancer spreads to the spine, a vertebra may fracture and collapse on itself causing back pain.

Cancer in the spine can also lead to pressure on the nerves in the spinal cord that causes weakness or numbness in the arms and/or legs.

Less often, the spread of breast cancer to bone releases excess calcium into the blood. High levels of calcium in the blood (hypercalcemia) can cause symptoms such as:

- Being very thirsty and urinating a lot.
- Constipation (difficult bowel movements).
- Loss of appetite.
- Being very sleepy.
- Confusion.
- Coma (this is rare).

Patients experiencing any of the symptoms of hypercalcemia should seek medical attention at once.

## Treating Breast Cancer That Has Spread to Bone

### 9. Q: How is breast cancer that has spread to bone treated?

**A: There are several effective ways to treat breast cancer that has spread (metastasized) to bone. The treatment used is tailored to the needs of each patient.**

Bone cancer in one location. If the cancer has spread to bone in only one spot, radiation may be given to treat the bone. In general, this will relieve the pain and prevent fractures at this site.

Bone cancer in several locations. If breast cancer has spread to several places in the bones, radiation treatment to all of the sites may not be possible because of limitations in the total amount of radiation that can be given safely. In this case, the patient may be given anticancer therapy with hormonal treatment or chemotherapy.

Pain relief treatment. Patients experiencing bone pain should be given pain medication. This may include nonsteroidal anti-inflammatory drugs (NSAIDs) and/or drugs containing opiates (narcotic pain killers). Radioactive therapy with strontium or samarium may also be used to treat painful bone tumors. Radiation or surgery may also be considered.

Drugs that help stop abnormal bone loss. Patients whose breast cancer has spread to bone may be given bisphosphonate drugs such as pamidronate (Aredia®), zoledronic acid

(Zometa®), and the drug denosumab (Xgeva®) to help slow or stop the cancer from destroying bone tissue.

Pamidronate, approved in 1995 by the United States Food and Drug Administration (FDA) for the treatment of breast cancer that spreads to the bone and myeloma bone disease. This bisphosphonate drug is given by intravenous (IV) infusion every three to four weeks and can be used with standard anti-cancer therapy.

Zoledronic acid, a stronger bisphosphonate, was approved by the FDA in 2002 for the treatment of cancers that spread to bone. Zoledronic acid is given by IV every three to four weeks and can be used with standard anti-cancer therapy.

Denosumab, approved by the FDA in 2010 is a drug that prevents bone breakdown or resorption by inhibiting RANKL, a protein that activates osteoclasts, the cells that are involved in bone breakdown or resorption. Denosumab is given by subcutaneous (under the skin) injection every four weeks and can be used with standard anti-cancer therapy.

## 10. Q: What is done when calcium released from the bone causes high levels of calcium in the blood?

**A: Most patients can be successfully treated with intravenous fluids containing saline (a salt solution) and intravenous bisphosphonate drugs.**

## Treatment-Related Side Effects

Advances in finding and treating breast cancer have greatly improved patients' survival rates. As a result, some patients receive anticancer therapies for longer periods of time, increasing the risk of side effects.

## 11. Q: What side effects can hormonal therapy and chemotherapy have on bone?

**A: Breast cancer treatment can lead to accelerated bone loss.** Bone loss is a fairly common side effect of some long-term estrogen-reducing therapies.

To understand the relationship between estrogen, breast cancer, and bone health, it is helpful for patients to know that:

- Estrogen, a hormone made by the body, plays an important role in maintaining good bone health. Estrogen makes bones stronger but can also make breast cancer grow. However, estrogen also makes some kinds of breast cancer grow. These are known as estrogen-receptor positive (ER+) breast cancers. Treatments that interfere with the way estrogen works can help prevent breast cancer tumors from growing and spreading. The problem is that this interference can also lead to accelerated bone loss.
- Hormonal therapy and chemotherapy are both breast cancer treatments that can cause bone loss due to their affect on estrogen.

Hormonal therapy with aromatase inhibitor drugs such as anastrozole (Arimidex®), letrozole (Femara®), fulvestrant (Faslodex®), and exemestane (Aromasin®) can block the synthesis of estrogen. These drugs are approved by the FDA for the prevention and treatment of metastatic disease. Aromatase inhibitors have been shown to be particularly effective in preventing breast cancer from recurring in post-menopausal women. However, in addition to suppressing estrogen and preventing cancer recurrence in post-menopausal women, aromatase inhibitors can cause especially severe bone loss and increased risk of fractures.

- Tamoxifen (Nolvadex®) is a drug that blocks the effect of the estrogen hormone. It can slightly increase bone mineral density in a postmenopausal woman, but is associated with bone loss in a premenopausal women.
- Chemotherapy can also cause bone loss and may increase the risk of fracture when the chemotherapy causes early menopause.

## **12. Q: What are the side effects of bisphosphonate drugs and denosumab?**

### **A: Short term side effects.**

#### **Bisphosphonate drugs.**

Short-term side effects that may occur immediately after receiving either pamidronate or zoledronic acid are:

- Flu-like symptoms such as fever, chills, and muscle aches. These side effects are often mild, do not last long, and tend not to recur following future treatments.
- Kidney function can be affected by IV bisphosphonate treatment. Accordingly, zoledronic acid or pamidronate should not be given to patients with severe kidney problems. In addition, breast cancer patients being treated with these drugs should have their kidney function checked before each infusion. This is done with a blood test that measures the level of a compound called creatinine.

#### **Denosumab.**

- Denosumab can cause lowering of the serum calcium level that can cause side effects such as lethargy and cardiac complications.

### **Long term side effects.**

The following long-term side effects have been reported in some cancer patients treated with bisphosphonates and denosumab:

- Osteonecrosis (dead bone) of the jaw is a rare dental condition. It is an area of exposed jaw bone that shows no sign of healing after eight weeks. The condition can cause a feeling of pain or numbness in the affected area.

As most cases of osteonecrosis of the jaw have occurred in patients treated with IV bisphosphonate drugs – mainly pamidronate and zoledronic acid – there is concern, but no proof, that the disorder is a side effect of these medications. Denosumab use has also been associated with osteonecrosis of the jaw.

Osteonecrosis of the jaw is much more likely to occur after an invasive dental procedure (such as having a tooth removed or dental implant surgery). This is why breast cancer patients should see their dentist for a careful dental examination before starting therapy with denosumab, pamidronate or zoledronic acid. If extensive dental work or oral surgery is needed treatment is usually delayed until after the dental work has been completed. Patients should also be sure to follow good oral health procedures (by, for example, regularly brushing and flossing their teeth). Additional information can be found in the Bone and Cancer Foundation publication “Osteonecrosis of the Jaw – Information for Cancer Patients” available online at [www.boneandcancerfoundation.org](http://www.boneandcancerfoundation.org) or by calling 1-888-862-0999.

## Preventing and Treating Bone Loss in People with Breast Cancer

### 13. Q: What can be done to reduce the risk of breast cancer treatment-related bone loss?

**A: There are several things that can be done to help prevent or slow the bone loss that can be caused by breast cancer treatment.** When such bone loss does occur, early diagnosis and treatment is essential.

Preventing/slowing bone loss. A healthy diet, regular exercise, and daily supplements of calcium and vitamin D can help prevent or slow cancer treatment-related bone loss.

Diagnosing bone loss. To make sure bone loss is identified quickly, some breast cancer patients should receive bone mineral density tests every 1 to 2 years.

Treating bone loss. Therapies for rapid bone loss include:

- Oral bisphosphonates such as alendronate (Fosamax®), ibandronate (Boniva®), and risedronate (Actonel®).
- Intravenous bisphosphonates (pamidronate, ibandronate and zoledronic acid\*).

\*Zoledronic acid used to treat cancer-related bone conditions is called Zometa®. Zoledronic acid used to treat osteoporosis and Paget’s disease of bone is called Reclast® in the U.S. and Aclasta® in other countries. The doses and schedule used to treat bone metastasis are different than those given to patients with osteoporosis or Paget’s disease.

- Denosumab\*\*

\*\*Denosumab used to treat cancer is called XGEVA®. Denosumab used to treat osteoporosis is called Prolia®. Prolia® is used as a treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for

breast cancer. Prolia® is given by subcutaneous (under the skin) injection every six months. The dose and schedule of denosumab used to treat bone metastasis is different than that given to patients with osteoporosis.

#### 14. Q: What can be done if breast cancer has weakened bone to the point where fracture is likely or has already occurred?

**A: Surgery or radiation therapy are two types of treatment that may be needed.** If a bone is thinned to the point where a fracture is likely, surgery may be necessary. For example, if an x-ray shows that a patient's hip is at high risk of breaking, hip replacement surgery may be required. In some cases, radiation treatments are used to help prevent fractures.

Preventing a fracture is easier and less painful than fixing a bone that has already broken. However, if a bone weakened by breast cancer does break or fracture, surgery or other procedures can be done at once to repair the bone.

### Health Care Professionals Who Can Help

#### 15. Q: Who treats patients whose bones are affected by breast cancer?

**A: One or more of a group of health care professionals may be involved.** Most often, the woman's **medical oncologist** (a doctor who specializes in treating cancer) and **breast surgeon** (surgical oncologist) plan the first approach to treatment. They are often helped by a **radiation oncologist** who is an expert in using radiation as a treatment for cancer.

Other health care professionals who may be involved include the following:

- **Orthopedic surgeons** play a role if there is a risk of fracture or if a fracture has occurred.
- **Neurologists and neurosurgeons** may be a part of the team if a tumor in the spine is causing pressure on nerves.
- **Physical medicine doctors** may prescribe physical therapy.
- **Endocrinologists** may be called upon if the patient has high levels of calcium in the blood or other metabolic issues.
- **Dentists or Oral Surgeons** play an important role in maintaining the health of the patient's teeth, gums, and jaw.
- **Oncology nurses, orthopedic nurses, and physical therapists** may help patients with the use of medications and physical therapy.
- **Mental health professionals** (such as **psychologists, social workers, or psychiatrists**) can help patients deal with the emotional and social impact of breast cancer. The use of talk therapy, with or without medicines for depression, can be helpful in many cases.
- **Gynecologists, internists, or additional health care specialists** may also be involved in managing a patient's care.

## Glossary

**Adjuvant therapy:** Hormonal therapy or chemotherapy given at the time breast cancer is diagnosed to decrease the risk of the cancer returning. Neo-Adjuvant therapy is when hormonal therapy or chemotherapy are given prior to surgery.

**Antibody:** A protein molecule that binds a very specific target.

**Biopsy:** Removal of a sample of tissue to be looked at under a microscope to check for cancer cells.

**Bisphosphonates:** Drugs used to prevent the breakdown of bone.

**Bone scan:** A test performed by a radiologist that allows the doctor to check the entire skeleton for the spread of cancer to bone.

**Chemotherapy:** Drugs that kill cancer cells.

**CT, MRI, and PET scans:** Special tests done by a radiologist that give a more detailed view of bone, nearby muscles, and other tissues.

**Herceptin® (trastuzumab):** A targeted treatment for women who have HER2-positive breast cancer.

**Hormonal therapy:** Hormones that change the environment of cancer cells in ways that can stop them from growing.

**Metastasis (plural: metastases, verb: metastasize):** The spread of cancer cells throughout the body. Cells that have spread to other parts of the body are the same as those in the original tumor. Lytic metastases are the thinned areas of bone that are found when cancer cells spread into and grow within bone tissue. Blastic metastases are the thicker-than-normal bone that may occur because of tumor growth or when a lytic bone metastasis heals.

**Osteonecrosis (dead bone) of the jaw:** An uncommon dental condition that is an area of exposed jaw bone that shows no sign of healing after eight weeks. The condition can cause a feeling of pain or numbness in the affected area.

**Osteoporosis:** Loss of and thinning of bone that increases the risk of fractures, especially in the spine, wrist, and hip.

**RANK Ligand:** A protein that activates osteoclasts, the cells that are involved in bone breakdown or resorption. Denosumab (Xgeva®/Prolia®) is a RankL targeted therapy.

**Radiation therapy:** Treatment with radiation to kill cancer cells.

**Tumor:** An abnormal mass of tissue. Tumors are either benign (noncancerous) or malignant (cancerous).

**The mission of The Bone and Cancer Foundation is to:**

- Provide information to cancer patients and family member on the causes and current treatment of cancer that involves the bone.
- Provide information and serve as a resource for physicians, nurses, and other health professionals regarding the management of cancer that spreads to the bone.



**The Bone and Cancer Foundation**

**Website: [www.boneandcancerfoundation.org](http://www.boneandcancerfoundation.org)**

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