

RADIATION FOR MELANOMA

By: Gil Lederman, M.D.

Melanoma is one of the dreaded skin cancers. It is the cause of an increasing death rate from skin cancer around the world. In many areas the increased rate of melanoma diagnosis is reaching huge proportions. Most researchers believe that sun exposure is the major risk. For those of us outside in the sun, good sun protection such as hats, clothing and sunscreen can help prevent this dreaded cancer. Being married to a dermatologist means never being far from the sun protection cream.

The first step is prevention. Of course, to many the issue is treatment of melanoma.

For those with melanoma a variety of treatments are available. These options have historically included surgery, radiation and chemotherapy. Of course it is best never to need treatment - that is to be prudent about sun exposure and aggressive about sun protection.

In a recent article by Bollo et al, published in the prestigious International Journal of Radiation Oncology, Biology and Physics, a question was asked about the need of radiation as additional treatment after surgery for melanoma that had spread to the lymph nodes in the axillary area.

Identified were eighty-nine patients treated between 1984 and 1999 that had axillary metastases from melanoma having surgery and radiation. Included were sixty-seven males and twenty-two females. The origin of the melanoma included head and neck area in three, trunk in forty-five, arms in sixteen and unknown in twenty-five. Patients' age ranged from twenty-three to eighty-nine with a mean of fifty-three years. Sixty-six of these patients had consultation for the first cancer occurrence in the axilla. Twenty-three were seen because of recurrent cancer in the axilla. All had melanoma.

Why were patients sent to be considered for radiation? Because they were felt to be at high risk for recurrence or re-recurrence in the axilla. Most of the patients considered had cancers greater than 3cm in diameter in the axilla - this included fifty-four patients. Forty-four patients had more than four positive lymph nodes. Sixty-nine patients had cancer beyond the capsule of the lymph node. Twenty-three patients had recurrent cancer after initial surgery. Seventy-seven patients had multiple risk factors.

The radiation was designed to include the axillary and supraclavicular areas while four patients received radiation only to the axillary area. The supraclavicular area is that part of the body by the clavicle or collarbone. This is an adjacent lymph node site. It often would be considered the next site for spread after the axilla.

Patients received 600 rad times five for a total dose of 3000 rad. Rad is a measure of radiation dose. This would be considered an unusual fraction schema. The most likely rationale is that melanoma is usually considered refractory to standard regimen which means low dose per treatment. This is a regimen similar to our hyperfractionated stereotactic radiation at Staten Island University Hospital, which is a very precise way of giving radiation to most any spot on the body. The beauty of radiosurgery is that it is a more accurate method of delivering radiation.

Follow-up for forty-six patients alive ranged from six to one hundred and fifty nine months with a mean of nearly five years.

At the time data was compiled forty-seven of eighty-nine patients developed relapse and forty-three patients had died. Their five-year actuarial survival rate was 50%. The time to development of distant metastasis was 6.6 months. Sites of distant cancer included the lung in twelve, brain in nine, skin in seven, bone in six and other sites ten. From a survival point of view, patients with

initial smaller melanomas as well as those in whom the axilla cancer developed more than eighteen months after diagnosis of the primary melanoma did better.

Of patients treated, only nine developed recurrence in the axilla. Thus the five-year control rate of the axilla was 87%. In the nine patients who had recurrence in the axilla the time to recurrence ranged from five to sixteen months with a mean of ten.

Included in the side effects was arm edema. Normally the fluids drain through the axilla to get back to the heart to circulate. Both surgery and radiation can interfere with lymph and blood return. This is most likely the cause of the arm swelling. There is an actuarial edema free survival rate of 71%. Twelve cases were felt to be transient with thirteen requiring medical intervention. One patient required surgical intervention for this complication.

The authors concluded, "From the current analysis it is not possible to comment upon the merits of hypofractionation versus conventional fractionation, although the nodal control rate was satisfactory. Nor is it possible to estimate its contribution to the risk of subsequent arm edema over that of surgery alone or surgery plus more conventional fractionation. For patients undergoing axillary dissection and radiation therapy for breast carcinoma, however, the incidence of arm edema ranges from zero to 56% (overall 26%). This broad range represents differences in the definition of arm edema, type of breast cancer therapy (lumpectomy versus modified radical mastectomy or sentinel lymph node biopsy versus axillary dissection), and the length of follow-up. Although our overall incidence of arm edema was 43% at five years nearly one half were transient or asymptomatic clinically, resulting in a symptomatic arm edema rate that is very similar to that reported in breast literature. Regardless the risk of arm edema must be weighed against the risk of distant failure and improvement in nodal control. The fact that nearly 50% of patients are alive and free of distant metastases at five and ten years demonstrates that axillary nodal metastases from malignant melanoma are not a hopeless situation. The avoidance of uncontrollable axillary nodal disease and ensuing pain, plexopathy, and unmanageable arm edema should therefore be one goal of curative therapy."

"Even after aggressive combined modality therapy, there is low nodal control and poor survival for patients with axillary masses greater than 6cm in size, more than two positive lymph nodes, Breslow thickness greater than 4mm, and axillary failure occurring within eighteen months from the diagnosis of the primary melanoma. These same patients have a 20% risk of requiring therapy for mild or moderate arm edema. Current research initiatives therefore should be aimed at the selective use of systemic agents and the intensification of local therapy in those patients with large nodal metastases, while modifying late toxicity, possibly through the addition of radioprotectors. In subgroup analysis, we were unable to show a significant improvement in any outcome through the use of any combination of systemic therapies. Given the small sample size, retrospective nature of the analysis, and the heterogeneous presentation of these patients, this finding is not entirely surprising and does not therefore disprove the benefit of immunologic or cytotoxic therapy. Despite this improvements in survival will require more effective systemic agents. Only then will the benefits of improved local therapy have a more than palliative, though significant, impact on the outcome of these patients."

Our data at Radiosurgery New York using hyperfractionated stereotactic radiosurgery for melanoma shows high control rates. Our control rate in the treated area is approximately 90%. This means 90% of the melanomas we treat require no further therapy in that area. Control means cessation of growth, shrinkage or disappearance of the involved cancer. Our technology allows us to treat melanoma essentially anywhere in the body.

Studies certainly are making progress for melanoma but it is much slower than any of us wishes.

What is interesting about melanoma is that it was historically thought to be a radio-resistant tumor. Now with high-dose, hypofractionated stereotactic radiosurgery we have learned that it is

one of the most sensitive tumors to radiation. Body radiosurgery allows us to treat new or recurrent metastases even after standard chemotherapy, radiation or surgery.

We have a panel of experts to evaluate scans. We ask for current scans, reports and a brief medical report. We have established a hot line at 212-CHOICES and as well, answer e-mail questions at gil.lederman@rsny.org.