This is “Is Breast Conserving Surgery an Option for BRCA Carriers Who Develop a Breast Cancer” and I’m going to argue the pro that this is in fact a reasonable and safe option. So the things that I’m going to talk about today are the risks of developing breast cancer in a BRCA carrier overall and the risks of developing a second breast cancer as well as, sorry. Recommendations for screening and risk reduction prior to the development of a breast cancer, risk of recurrence after breast conserving therapy, alternative risk reduction methods to more extensive surgery for patients who choose breast conserving therapy or BCT, and overall survival which we probably would agree is the ultimate goal of therapy.

So when we look at BRCA risks, BRCA1 patients have about an 80% chance probably closer to 87% lifetime risk if they live to a ripe old age of 85 of developing a breast cancer. If they are to develop a single breast cancer and don’t have maximal therapy bilateral mastectomy, their chances of developing a second breast cancer is about 60% and their ovarian cancer risk is 40%. The rates are pretty similar with BRCA2. So knowing that what do we recommend to young women who have a BRCA mutation in terms of screening and risk reduction? So if you look at the NCCN guidelines they discuss breast awareness at the age of 18 although I think we will all argue that most young women are aware of their breasts before age 18. Clinical breast exam every 6-12 months beginning at age 25 as well as MRI and mammogram yearly at age 25 and whether those are staggered or performed together is still a matter of debate, and also to consider prophylactic surgery such as bilateral prophylactic mastectomy or oophorectomy.
So how does this risk reduction work? If you do a bilateral salpingo-oophorectomy not only does it reduce your risk of ovarian cancer quite significantly, but it reduces your risk for breast cancer by about 50% in a BRCA carrier. If a BRCA carrier undergoes a bilateral mastectomy it reduces it by 90% which it’s a shock to most patients that it’s not 100% so that’s something to keep in the back of our minds as we move forward. When we look at surveillance or chemo prevention with a drug like Tamoxifen there’s really no effect for BRCA1 carriers whereas there is effective risk reduction in BRCA2 carriers with Tamoxifen.

So once a patient develops a breast cancer, how do we treat it? When we talk about surgical intervention we always talk with the patient about BCT, Breast Conserving Therapy or what we call a lumpectomy or a mastectomy. And there are some reasons that some patients are going to have a tumor that’s more amenable to one versus the other. If we look here at MRIs we see this is a fairly small tumor in comparison to the size of this woman’s breast, we don’t see a whole lot else going on in her breast. This woman however has a very large tumor and upfront de novo she’s a poor candidate for breast conserving therapy. There are certain things we can do to improve that candidacy but this is a patient who’s less likely to achieve breast conserving therapy.

So if they are a candidate for breast conserving therapy due to other factors, what is their risk of recurrence after breast conserving therapy? So when we look at BRCA carriers who have had breast conserving therapy their risk of ipsilateral breast cancer recurrence, so cancer recurrence in the same breast, is actually statistically equivalent to those who have sporadic breast cancers at about 15 years. However, the contralateral breast cancer risk is quite significantly increased over a woman with a
sporadic breast cancer with a hazard ratio of 9.57 at 15 years. And actually that bumped up to a little bit over 10 if you read the manuscript. When we look at several articles that have discussed this issue, we see again in breast tumor recurrence there are some that found a small increase of risk of in breast tumor recurrence after breast conserving therapy in BRCA carriers. But all of them found an increased risk for contralateral breast cancer in that population.

Which brings us to the question of because of this contralateral breast cancer risk does every woman who has a BRCA mutation and a cancer in one breast, require a mastectomy in the other breast and a mastectomy on that breast? And I would say no there are alternative risk reduction methods for those who choose breast conserving therapy, the same paper by Pierce, et al., looked at the effect of oophorectomy on recurrence risks and what they found is that once again ipsilateral tumor recurrence was non significantly different so essentially statistically equivalent in contralateral occurrence of a breast cancer although again statistically increase was cut in half. So oophorectomy is an effective risk reducing method.

When we look at the effect of drug therapies what we see are here Tamoxifen, so endocrine therapy, oophorectomy and chemotherapy and you see that all of them provide a significant risk reduction for patients who have a unilateral breast cancer with a BRCA mutation in their contralateral breast cancer risk. So not only surgery, but medical interventions can increase their risks of a second breast cancer.
Now when we look at things like screenings, certainly screening is not going to prevent a second breast cancer but does it catch it at an earlier stage. And we look at this cohort that had MRI and mammography or MRI only and what you see are a clustering of tumors at very small stages, so very small tumor stages typically a centimeter or less. So although screening cannot decrease their risk of getting a breast cancer it certainly decreases their risk that you’re going to have a large breast cancer at the time of presentation.

So really the ultimate goal the gold standard here, overall survival, that’s what everyone wants to know is doc if I choose one therapy over the other do I have a higher likelihood of dying. And unfortunately there, all we hear is a lot of crickets, there’s not a whole lot of good available data for the difference in overall survival for these patients. There are some sort of historical studies that we can look at in all comers that tell us about a patient who has a second breast cancer and what their risk of dying is from that second breast cancer. So certainly when we look at in breast tumor recurrence we can go back to Fisher et al., and NSABP06 which established the equivalence of breast conserving therapy to mastectomy and what you see here is when we look at lumpectomy patients, patients who have lumpectomy alone and no other intervention versus lumpectomy plus radiation, we all know that lumpectomy plus radiation reduces the risk of developing an in breast tumor recurrence by about 50%. So the patients who did not undergo radiation had a much higher risk of in breast tumor recurrence. However when you look at their survival, and here they’ve added mastectomy to the group, you can see that those lines are one on top of the other. So regardless of the increased risk for in breast tumor recurrence, there was no difference that was statistically
significant in overall survival. So despite the fact that they recurred, their overall survival was exactly the same.

And we can see this more specifically in the BRCA cohort. So when they look at BRCA carriers who elect to have contralateral prophylactic mastectomy versus not, you can see that the patients who have what we call a CPM or contralateral prophylactic mastectomy, have a significantly higher cancer specific survival, but their non cancer survival is fairly equivalent especially in these lower age ranges, 18-49 and 50-59 years. And really most importantly when we look at the study by Narod et al, we see that patients who die of their breast cancers BRCA patients who die of breast cancer are much, much more likely to die of their first cancer as a consequence of their first cancer than any subsequent breast cancer they are to develop. So although a contralateral prophylactic mastectomy or a mastectomy of the same side reduces risk of recurrence, it really has very little effect on overall survival or disease specific survival.

So when we look at the conclusions here, BRCA1 and 2 mutations significantly increase the risk of breast cancer we all know that. Breast conserving therapy in BRCA carriers does lead to an increased contralateral breast cancer risk, it may lead to an increased risk of in breast tumor recurrence but likely not, that risk can be reduced through many other methods; oophorectomy, endocrine therapy and chemotherapy. And mortality is likely determined more by your first breast cancer rather than any other subsequent breast cancer that is to occur.
So is it safe, that’s the big question, doc is it safe for me to do this? When we look at the medical definition of safe we see that it’s not causing harm or injury especially having a low incidence of adverse reactions and significant side effects when adequate instructions for use are given and having a low potential for harm under conditions of widespread availability. So it’s tough to apply that to the BRCA carrier but really when you look at it they talk about adequate instructions and low potential for harm. So I think when we talk about safety we have to talk about the patient’s identification of what safety is. So when you adequately explain to a patient that they have an increased risk of contralateral breast cancer which may require a second operation but likely will not hurt their overall survival and they are willing to undergo other interventions to reduce their risk, and intensive screening to catch a second potential breast cancer early, then yes I think that we could consider this under this definition safe, after adequate instructions have been given.

So just to break this down, just a real simple, quick and dirty review, so when we look at a patient, a patient’s risk for in breast tumor recurrence, she’s a BRCA carrier and she’s had a unilateral breast cancer, if she undergoes breast conserving therapy her in breast tumor recurrence is likely the same if not potentially slightly increased due to when you look at the studies. When you look at someone who has breast conserving therapy plus some sort of systemic therapy or risk reducing surgery, their risk is exactly the same. Obviously if they were to have a unilateral mastectomy their risk of in breast tumor recurrence is really nil, very low. And their bilateral mastectomy, if they were to undergo that, their in breast tumor recurrence is really not applicable.
When we look at contralateral breast cancer risk that’s when things really get different. Much increased for patients who undergo breast conserving therapy, slightly decreased well slightly or significantly decreased by about ½ in patients who undergo adjuvant therapies. If they have a unilateral mastectomy their risk is no different from the breast conserving therapy population. But when we look at death like I said, we’ve got big question marks here, some people say increased risk, some people say decreased risk, but when you look at the, sort of the risk of dying of your second breast cancer, we see that it’s potentially very low.

So what do the experts say? I’m certainly an expert but I’m not the expert, so let’s look at the heavy hitters here. So Nature, what’s Nature say? Nature says in terms of BRCA carriers so for the treatment of established breast cancer, breast conserving therapy is indeed a reasonable option. British Medical Journal it’s pretty much the same thing, breast conserving surgery is safe in selected woman with a BRCA mutation when combined with adjuvant therapy. Annals of Surgical Oncology, there is no standard treatment for BRCA carriers with a diagnosis of breast cancer, these women might benefit from an extensive procedure at the time of surgery but data are still limited. And the European Journal of Cancer says breast conserving therapy remains today, a reasonable option for genetically predisposed breast cancer patients.

So you know I asked another group of experts is it safe and well they all said yes. So I’ll leave it to Dr. McAuliffe to try to convince you otherwise.