Hello, I’m Doctor Kandace McGuire and I’m going to talk to today about screening and surgical options for high risk patients for breast cancer. I have nothing to disclose.

The objective of today’s presentation are that the listener to the presentation will be able to compare the sensitivity and specificity of breast MRI and mammography in detecting breast cancer in a high risk population. Also to identify which patients are eligible for high risk screening with modalities such as MRI and to discuss with patients with high familial risk their potential risk reduction with bilateral prophylactic mastectomy.

First we’ll talk about who is eligible for screening, what kind of screen they’re eligible for and when that screening should begin. The National Comprehensive Cancer Network guidelines suggest that patients at high risk should start screening at age 25. They should begin with clinical breast exams every 6 to 12 months and some sort of imaging every 12 months. The question is what imaging is best, is standard mammography adequate, should we add MRI or perhaps screening ultrasound?

If we look at screening mammography there are several advantages. There have been many randomized control trials that suggest it has an advantage over no screening that have taken place since the 1960s. But we’ve shown a reduction in mortality for breast cancer in about 25 to 30 percent of patients. And we in general find smaller and more node negative tumors. However, there’s no such thing as a normal breast and we don’t find that there’s a normal breast on imaging across many patients. Breast tissue not only varies amongst patients but within a patient due to hormonal changes. And there are several disadvantage to two-dimensional imaging. Also, we only
have anatomic information for mammography, we don’t have anything that talk to us about the physiology of the breast.

As you can see here the breast changes with age even within the same patient. When they are younger we have a significantly denser breast. As the patient becomes older the breast becomes less dense and easier to screen with mammography.

For patients at high risk for breast and ovarian cancer who are screened at a young age, we find a fairly high rate of interval cancer detected by palpation in approximately 35-50 percent of patients, this is how they present. Unfortunately, tumors of greater than 1 cm in size in about 40 to 78 percent of those patients and 20 to 56 percent of them had nodal involvement at the time of their presentation.

We’ve looked at other screening modalities to improve our sensitivity and increase our uptake of early breast cancers in these patients. Several studies have suggested that ultrasound and MRI could be better modalities for this patient population. If you look at this screen here we see that mammogram is compared to ultrasound and MRI in several studies. And what we see in terms of sensitivity is that MRI is significantly better than mammogram and ultrasound in detecting early breast cancer.

Unfortunately, MRI is not nearly as specific in all studies as mammogram. Ultrasound falls somewhere in between. And thus it is typically, it’s typically recommended that patients undergo
MRI and mammography together. Those who are recommended to have annual MRI screening based on evidence in the literature are patients with BRCA mutations, untested relatives of BRCA carriers and those with a lifetime risk of breast cancer that is gauged to be 20 to 25 percent or greater based on a model that uses family history.

Those who are recommended to have MRI based on an expert consensus opinion are those who’ve had radiation into their chest wall in the past or those with other syndromes such as Li-Fraumeni, Cowden and Bannayan-Riley-Ruvalcaba Syndrome. Also their untested first degree relatives would be eligible for a screening.

The patients in whom we have insufficient evidence to recommend MRI are those with a lifetime risk of 15-20 percent, those with lobular carcinoma in situ, those with atypical ductal hypoplasia, patients simply with dense breast tissue and those with a personal history of breast cancer. There are certainly patients in whom we know MRI is of no help and those are patients with a less than 15 percent risk of lifetime breast cancer.

So for those patients who we recommend MRI and mammography we recommend that it is done either together or in 6 month intervals alternating. Unfortunately this is still a controversial issue amongst breast imagers. For those patients who cannot get MRI for some reason we do recommend ultrasound in addition to mammography. However, MRI is still considered the gold standard.
So why is MRI so much better than mammography? We look here at a 41-year old patient who has a BRCA1 mutation. This is her annual screening mammography with state of the art digital mammography. Really we see no difference between the right and the left breast. However when we add ultrasound to the picture we do see the suggestion of perhaps a mass. And when we look at MRI we see what is obviously an early breast cancer within her breast.

Again another patient with a completely normal mammogram on the right breast. And here we see within her right breast actually a fairly large breast cancer. So those are the patients who are eligible for screening and that is how we screen them. Unfortunately for some patients screening is just not enough and they request or require risk reduction surgery. There’s no single definition or a patient who is quote unquote high risk enough for risk reducing surgery. Again, the NCCN does guide us and recommends this sort of surgery in patients who carry a BRCA mutation or another mutation such as P-TEN or Li-Fraumeni, those with a compelling family history who might be tested BRCA negative or those who have lobular carcinoma in situ. This surgery is most commonly requested by BRCA mutation carriers.

The first paper to discuss risk reduction with prophylactic mastectomy was a study by Hartman et al in the New England Journal of Medicine in 1999. This was the study performed at the Mayo Clinic from 1960 to 1993 almost 700 women underwent risk reducing surgery. The most common surgery performed was a subcutaneous mastectomy what we’ll later discuss is a nipple sparing mastectomy. However, in the later years of the study simple mastectomy was performed.
In the moderate risk group of patients we got a 90 percent risk reduction. In the high risk group we found an ever greater risk reduction of almost 95 percent. In another study by Rebbeck et al we can see that patients with a BRACA1 mutation who undergo bilateral prophylactic mastectomy have a very low risk of contracting breast cancer. However those who did not undergo bilateral prophylactic mastectomy have a significant risk of developing breast cancer over the next 10 to 30 years of their life.

So why isn’t everyone rushing out and getting mastectomy. Well there are certainly problems with the surgery. It’s not a benign procedure, there’s time in the hospital, there’s time for a followup, there’s time lost from work and family. There’s risks to the surgery. It’s not a risk-free procedure. There can be risks of bleeding, there can be cosmetic risks and there can be risks of infection. And there’s always a risk that one could contract breast cancer despite risk reducing surgery. And as I mentioned before the cosmetic outcome can sometimes be less than pleasing.

What we’ve developed in the past few years is something called skin sparing mastectomy where the grand majority of the skin of the breast is preserved and the breast can be reconstructed with an implant or with tissue from elsewhere on the patient’s body. As you can see here this patient has had an excellent cosmetic outcome. We can also see this in a patient who’s had tissue transfer to reconstruct her breast.

One of the latest advances is nipple-sparing mastectomy. This is a surgery that was previously done in the 1960s and 1970s. However, a difference in surgical techniques cause these patients to have a
high risk of recurrence of breast cancer and that’s, the technology was abandoned for several years. Somewhere in the 1990s to the early 2000s the technology was revived and patients are now undergoing nipple sparing or total skin sparing mastectomy with excellent results.

Here we can see several studies suggest that the recurrence in the nipple and areola complex are extraordinary, usually zero to one percent. And overall occurrence of breast cancer is also extraordinarily low, anywhere from zero to less than ten percent. This is basically equivalent to a skin sparing mastectomy or a standard total mastectomy.

So who is right for a nipple sparing mastectomy? The patients that we’re talking about today are the prophylactic mastectomy patients and they are an ideal candidate for this surgery. Not every patient undergoing prophylactic mastectomy though from a cosmetic aspect is a good candidate for nipple sparing mastectomy. Patients who are a good candidate for this surgery are typically younger, they have no history of prior breast surgery or breast surgery that involves incisions in and around their nipple and their areola. They’re non-smokers, their fairly thin with a BMI less than 30, they have no ptosis to their breast so the breast does not have any sort of droop, the nipple is at or above the inframammary fold. And the breast size should be approximately a C cup or less. Certainly there are exceptions to these rules, very young patients who have larger than a C cup but have good skin turgor are good candidates for this operation. There are also some relative contraindications, if the patient has had a history of breast cancer and has had radiation to that area then they become a less optimal candidate.
So the question is what is the outcome of this surgery, is it equivalent to skin sparing mastectomy? If patients are going to undergo a large operation, what is the benefit they’re going to derive? Well we’ve already talked about the fact that the outcomes are equivalent in terms of cancer risk reduction. However, there can be risks to leaving the nipple in place. And those include nipple necrosis. This is less than 10 percent in most studies. And there are definitely contributing factors to that. Patient age can be a contributing fact, prior radiation, a recent history of smoking and perhaps even incision placement. Luckily, most patients who experience nipple necrosis do not lose their nipple. We can use expectant management to nurse them through unless there’s a risk of implant exposure or involve breast infection.

Unfortunately nipple sensation is something that we still don’t know whether this is going to be preserved or not in the patients with nipple-sparing mastectomy. It’s not widely studied and small studies we find that almost 70 percent of patients report some loss of sensation and 14 percent report a total loss of sensation. In terms of patient satisfaction in cosmetic outcome we know that there can be problems with nipple sparing mastectomy. The nipple can become malpositioned particularly in patients with large breasts or significant ptosis. And there can be a loss of projection of the nipple areola complex or pigmentation over time. However most patients reported good cosmetic outcomes at 48 months and their overall satisfied with the surgery and its outcome.

So what are our outcomes here? This is a patient who unfortunately did have a breast cancer and opted for a nipple sparing mastectomy bilateral with a tissue expander reconstruction. When she did get her final implant six months later she’s had an excellent cosmetic outcome and is very happy.
This is another patient who underwent risk reducing surgery for a BRCA mutation just like the patient we’re talking about today. She is an optimal candidate with a lower BMI, minimal ptosis and a smaller breast size. She actually underwent reconstruction with tissue transfer, you can see her scar down her below from her transverse rectus abdominis flap. As you can see she’s also had an excellent cosmetic outcome. Her incision just like the patient before her are placed underneath the breast so that there’s really no way that you can tell that they’ve had surgery if they’re looking down.

This extremely important to patients especially in the prophylactic population. So really those are the patients who are eligible for risk reducing surgery and those are the patients who are eligible for a screening. I hope today that we’ve discussed those options and that you’ll be able to counsel your patients as to the next step after mutation has been detected. Thank you.