

IMPLICATIONS FOR PLASTIC AND RECONSTRUCTIVE SURGERY STEPHEN BAKER, M.D., D.D.S. EXPLAINS

The word, plastic, comes from *plastikos*, the Greek word to restore to normal, reform, rebuild or remold, and that's what we do in plastic surgery. We try to restore abnormal to normal. Many of the abnormalities that we see as plastic surgeons are related to breast cancer, head and neck cancer, trauma, or birth anomalies. All of these people want to look normal, and one of the ways we can make them look normal is to add tissue volume to correct deficiencies or asymmetries.



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For instance, in facial reconstruction, I have patients who have had significant accidents where fat gets trapped or injured leading to the scarring and atrophy that results in facial asymmetry. Also, I have patients who are born with congenital facial asymmetry. The ability to reliably use grafted fat as a reconstructive tool allows the surgeon the ability to obtain the same result as that achieved by much more invasive operations. So rather than doing a major operation, I can literally take fat out of the patient's abdomen, thigh, buttock, or wherever they have a little extra, and inject it in areas where they are deficient.

Fat grafting has obvious applications to cosmetic surgery as well. Years ago, the standard facelift was all about "pulling, cutting, and tightening the face." As our sophistication with facial analysis and aesthetics has improved, we find that it's not just about pulling skin tighter, it's about repositioning tissue to where it was in the patient's youth and restoring the volume of soft tissue lost to the atrophic changes of aging. So now we put less emphasis on just tightening and much more on properly repositioning and restoring volume.

The facial rejuvenation techniques I currently use are those that reposition deeper soft tissues and restore soft tissue volume. As a material to restore lost soft tissue volume, grafted fat is potentially the ideal filler. It is your

own tissue, inexpensive, biocompatible, abundant, and when it takes, permanent. Additionally, it ages well, meaning that it always has a normal, natural consistency. The only problem keeping fat from being dubbed the ideal filler is that it is unpredictable in terms of how much stays over a long period of time. Typically anywhere from 30 to 50 per cent of it will be maintained after one injection, but obviously that means you need three or four injections to get to your final goal.

In our study, we had almost zero fat graft resorption when we put human fat and NPY in nude mice and observed them over three months. When we compared that to human fat put in mice without NPY, we saw about 70 per cent resorption. So we saw a profoundly enhanced effect on the reliability and predictability of fat grafting when it was used in conjunction with NPY.

Even more interesting than NPY's ability to maintain the predictability of grafted fat is its ability to generate de novo synthesis of fat in response to the NPY. If we placed NPY under the skin of a mouse or a monkey without any added fat, we found that we generated a little fat pad. It is our hope that we may be able to take this technology one step beyond fat grafting and enable us to create de novo adipogenesis and bypass the need for grafted fat. That will be the subject of our next NIH grant.

Finally, in contrast to fat grafting by stimulating the receptor, we found that blocking the NPY2 receptor leads to adipolysis. This means that we are able to deliver a subcutaneous injection to the animals and they lost fat. No adverse effects were found in any of the animals, and the pathway through which this works is very similar throughout all types of animals, including humans. We are collaborating with partners to develop a drug that can safely be given to humans to eliminate fat without surgery. I would not expect it to replace liposuction, but it would be a convenient alternative. Our next steps on this work are to do the preliminary work that is necessary prior to an FDA new drug application. The most exciting aspect of this research is that it truly represents the NIH "bench to bedside model" of collaborative, translational research. It is very exciting to have the opportunity to potentially make a major contribution to the field of plastic surgery. ■