Eighth IQUAM Consensus Conference Position Statement: Transatlantic Innovations, April 2009

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**Background:** On April 7, 2009, the International Committee for Quality Assurance, Medical Technologies and Devices in Plastic Surgery (IQUAM) issued its 8th Position Statement. IQUAM is a professional medical and scientific organization committed to the surveillance of existing and new technologies and devices in plastic surgery. IQUAM periodically reviews and evaluates updated international literature and studies and scientific data, and recommends standards of treatment for plastic surgery devices and technologies. IQUAM proscribes potentially deleterious use of products, devices, and technologies, or their unintended application or application for unsuitable indications.

**Methods:** Presentations of an international panel of experts made during the Transatlantic Innovations Symposia in Paris, in April of 2009, were reviewed by an advisory board that prepared the position statement for distribution to plastic surgeons and regulatory bodies. The advisory panel was international in nature and included plastic surgeons with expertise in the specific areas evaluated.

**Results:** Three clinical areas of greatest concern to plastic surgeons were evaluated for efficacy and safety: silicone breast implants, tissue engineering, and injectable therapies.

**Conclusion:** Specific recommendations designed to increase clinical safety and patient education for informed consent were made in each area. (*Plast. Reconstr. Surg.* 127: 1368, 2011.)

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**BREAST AUGMENTATION AND RECONSTRUCTION**

The purpose of breast augmentation and reconstruction is to improve the psychological and physical condition of the patient. The breast augmentation method should be chosen depending on the needs of the patient and the compatibility in the individual case.1–5

**Silicone Breast Implants**

A. Since IQUAM’s former declarations, silicone implants filled with either silicone gel or saline, textured by various methods or smooth surfaced, or covered by polyurethane, continue to be widely used internationally for breast implantation, with the types varying by geographic region.

B. Additional medical studies have not demonstrated any association between silicone gel-filled breast implants and carcinoma or any metabolic, immune, or allergic disorder. These studies reconfirm prior data.6–11

C. Silicone gel-filled breast implants do not adversely affect pregnancy, fetal development, breast-feeding, or the health of breast-fed children.6,12–14

D. Further changes in implant structure and composition need to be evaluated.

**Autologous Breast Reconstruction and Augmentation Techniques**

Surgical methods for breast reconstruction and augmentation with autologous tissue such as microsurgical tissue transfer from various donor areas and extent, pedicled flaps, and local flap techniques undergo constant reevaluation and are well established according to individual indi-
cations and conditions. They have been used in combination with silicone breast implants without specific inherent complications reported.\textsuperscript{15–19}

**Autologous Fat Grafting**

Fat grafting for soft-tissue defects has been performed for approximately 40 years with a low complication rate. Ongoing studies show promising results of fat grafting procedures for breast reconstruction and augmentation. There is clear evidence that the volume and take of fat grafts can be increased by the preoperative and postoperative use of a vacuum device. More studies are required to evaluate the efficacy and optimal duration of vacuum application.\textsuperscript{20–23}

**Other Injectables for Breast Augmentation**

New alternative materials and methods, such as exogenous injectables, and recently also stabilized hyaluronic acid and therefore potentially fully resorbable products, are under review.\textsuperscript{24}

**General Recommendations for Breast Augmentation and Reconstruction**

A. IQUAM believes it is important to advise patients of potential hazards and risks, the possible need for reoperations, and the benefits of breast augmentation or reconstructive surgery. A detailed and updated patient information and consent form must be provided and discussed with the patient before surgery.

B. A reasonable length of time should be allotted after consultation for the comprehension and evaluation of data before the decision to undergo surgery is made.

C. It is recommended that breast augmentation surgery be postponed until after the age of 18 years. Such a procedure in teenagers requires in-depth evaluation of motivation and emotional and physical maturity before surgery is considered, even in medically indicated cases.

D. Patients with breast implants should be encouraged to have regular and long-term follow-up, preferably by the operating surgeon.\textsuperscript{25,26}

E. No definite length of time has yet been defined for the longevity of breast implants. Routine replacement of implants is not recommended. The indications for replacement should be based on specific patient indications.

F. IQUAM calls for continuous clinical and scientific research for documentation and monitoring of breast implants and patients by means of a national and/or international registries.

G. Advertising of breast implant procedures should be restricted to the medical aspects of the operation and presented in a professional, dignified way and without exaggerated claims.

H. IQUAM calls for the approval of silicone gel-filled breast implants for global clinical use and unrestricted availability to all patients.

**TISSUE ENGINEERING AND WOUND HEALING**

Tissue engineering holds the promise of generating tissues de novo. Adipose tissue is the ideal soft-tissue surrogate with which to redefine body contour defects because of its intrinsic plastic characteristics.

**Stem Cell Therapy**

One of the most exciting frontiers in medicine today is the use of stem cells. Unlike the controversial evaluation of embryonic stem cells, adult stem cells derived from adipose tissue are easily available without ethical controversy. The following guidelines should be respected:

- The injections should be performed in the same operative session as the liposuction procedure to remove the fat.
- The stem cells should have been only minimally manipulated.
- The stem cell–enhanced fat transfer should not alter the original relevant biological function of the stem cell.
- The therapeutic use of autologous stem cells is not submitted to drug therapy regulations.
- Reinjection of autologous stem cells in a separate session therefore is not recommended.

For over a decade now, it has been shown that successful autologous fat grafting is highly dependent on the techniques used for extraction (liposuction at low negative pressure), processing (centrifugation and decanting of the extracted fat), and reinjection to result in a high concentration of adult stem cells, producing long-lasting results and even therapeutic effects in injured tissues. Indications for stem cell–enhanced adipose tissue transfer under the above conditions include augmentation of the subcutaneous layer (e.g., for defects following lipo-
suction complications or other acquired tissue defects, such as in the face, breast, gluteal area, hips, thighs, or the dorsum of the hands).

Under investigation to date are treatments of radiotherapy injuries and breast reconstruction following cancer. Stimulated by our experience with fat grafting, numerous basic laboratory and animal model studies are underway in many parts of the world.26–32

Regenerative medicine is a promising road for future advancements in plastic surgery. Laboratory-engineered constructs must consist of safe components before implantation in patients. Institutions such as the European Committee for Standardization are setting strict measures.33–36

Growth Factors

An increasing number of growth factors are becoming commercially available for an ever wider range of indications, either as therapeutic agents or adjuncts per se or as elements of tissue-engineered constructs. IQUAM is warning against the indiscriminate application of growth factors before undesired side effects (e.g., uncontrolled cell divisions, malignancies) have been diligently studied in the short and long term after their application. Notified bodies issuing CE marks should be aware of this and stress that only temporary CE marks are being granted while awaiting longer term studies.37,38

Shock Wave Therapy

Recent studies suggest that extracorporal shock wave therapy, originally developed for resolution of kidney stones, is useful in the treatment of chronic wounds, burns, and tendinopathies. More studies are needed to evaluate the frequency and duration of application. It is likely that more indications will be suggested in the future.39–41

INJECTABLE THERAPIES

Lipolysis or Lipodissolve Injections by Phosphatidylcholine Derivatives

Phosphatidylcholine has been used for various clinical indications for many years. Phosphatidylcholine is currently being used off-label for dissolving fat in clinical aesthetic applications. Data concerning the efficacy, outcome, and safety of its use have not yet been established. Further basic science and clinical trials should precede the use of this drug for aesthetic application. Premarket approval trials are underway.42–45

Botulinum Toxin Type A

Botulinum toxin type A has been used extensively for aesthetic purposes. Botulinum toxin type A in high dosages has been used in various therapeutic clinical applications, with minimal reported significant adverse effects. Current clinical data confirm the safety of botulinum toxin type A for aesthetic indications when used by experienced doctors under medically acceptable conditions. Patients should be provided with detailed information, and a signed informed consent should be obtained before the procedure is performed (Fig. 1).

Injectable Fillers

Today, more than 35 percent of the procedures performed by plastic surgeons are no longer purely surgical. The use of resorbable substances is preferable to the use of nonresorbable fillers, as recommended by many national health authorities and academic societies. Furthermore, IQUAM stresses that degradability should be discerned from resorbability. Permanent fillers (excluding autogenous tissue) can give a definitive correction but have been reported to be associated with long-term irreversible complications and should be used with extreme caution.46

Risks depend on the nature of the implant and the volume, depth, and site of the injection, especially in permanent substances, but also in resorbable products. The patient’s history and the long-term follow-up are important for documenting allergic or late reactions. Most important is the risk-to-benefit ratio for each product, as the perfect material does not exist. IQUAM recommends reporting complications of fillers to regulatory bodies and mandatory registration of adverse effects associated with injection of fillers to better estimate the extent of complications.47–49

Collagen Fillers

Collagen-derived soft-tissue fillers with a bovine origin have lost their importance and have not been subjected to any chemical or manufacturing changes in recent years because of the prevalence of other substances. Most of the available products are obligatorily subjected to be used only after a negative allergy skin test at least 6 weeks before injection. This is not the case for porcine-derived products, which have not shown different efficacy or local complications such as infection, granuloma, nodule formation, or visibility through the skin. Allergies have not been reported so far.50–53
Addendum I

BOTULINUM TOXIN TYPE A INFORMED CONSENT *
(Botox Cosmetic)

Botox is made from Botulinum Toxin Type A, a protein produced by the bacterium *Clostridium botulinum*. For the purpose of improving the appearance of wrinkles, small doses of the toxin are injected into the affected muscles blocking the release of a chemical that would otherwise signal the muscle to contract. The toxin thus paralyzes or weakens the injected muscle. The treatment usually begins to work within 24 to 48 hours and can last up to four months. The Food and Drug Administration (FDA) approved the cosmetic use of Botulinum Toxin Type A for the temporary relief of moderate to severe frown lines between the brow and recommends that the procedure be performed no more frequently than once every three months.

It is not known whether Botulinum A Toxin can cause fetal harm when administered to pregnant women or can affect reproductive capabilities. It is also not known if Botulinum A Toxin is excreted in human milk. For these reasons, Botulinum A Toxin should not be used on pregnant or lactating women.

I authorize and direct _________________________, M.D., with associates or assistants of his or her choice, to perform the following procedure of Botulinum A Toxin injection(s) on ___________________________. (Patient Name)

_ The details of the procedure have been explained to me in terms I understand.
_ Alternative methods and their benefits and disadvantages have been explained to me.
_ I understand that the FDA has only approved the cosmetic use of Botulinum A Toxin for frown lines between the brow. Any other cosmetic use is considered off label.

_ I understand and accept the most likely risks and complications of Botulinum A Toxin injection(s) include but are not limited to:

  *paralysis of a nearby muscle that could interfere with opening the eye(s)*
  *local numbness*
  *headache, nausea, or flu-like symptoms*
  *swallowing, speech, or respiratory disorders*
  *swelling, bruising, or redness at injection site*

_ I understand and accept that the long-term effects of repeated use of Botox Cosmetic are as yet unknown. Possible risks and complications that have been identified include but are not limited to:

  *muscle atrophy*
  *nerve irritability*
  *production of antibodies with unknown effect to general health*

_ I understand and accept the less common complications, including the remote risk of death or serious disability, that exist with this procedure.

_ I am aware that smoking during the pre- and postoperative periods could increase chances of complications.

_ I have informed the doctor of all my known allergies.

_ I have informed the doctor of all medications I am currently taking, including prescriptions, over-the-counter remedies, herbal therapies, and any others.

_ I have been advised whether I should take any or all of these medications on the days surrounding the procedure.

_ I am aware and accept that no guarantees about the results of the procedure have been made or implied.

Fig. 1. Botulinum toxin type A informed consent, provided by The Doctors Company, USA.
Hyaluronic Acid Fillers

Commercially available hyaluronic acid fillers have a wide variety of properties that have an extensive impact on their use and clinical outcomes. Combining objective factors that influence filler chemistry with clinical experience will improve patient care, make optimal results more likely, and should decrease complications.

Not all hyaluronic acid fillers have stood the test of time, and the popularity of some has decreased. Regulation of these injectables varies widely from country to country, and approval is often gained after short-term studies of 1 year or less. To avoid confusion in the use of materials, IQUAM recommends that users verify the validation of the CE mark or U.S. Food and Drug Administration approval before clinical use.

Continued long-term postmarketing surveillance by both industry and notified bodies is essential. Physicians should stay alert to detect late adverse events and report these to the competent authorities. Patients and users need to be given updated information on the risks of these materials. Supply of injectables should be limited to trained physicians.

However, appropriate guidelines are often lacking, and as their clinical use expands rapidly,

* Provided by The Doctors Company, USA.

Fig. 1. (Continued)
there is considerable overlap in application. More choices demand greater clinical judgment and continuing clinical trials to highlight the differences, the safety, the efficacy, and the evolution of the use of these materials.

Cross-Linked Polyacrylamide Hydrogel

Permanent fillers based on acrylamides have been in clinical use for more than 15 years. The current European manufacturer has attained CE certification with the remaining monomer content as below 2 ppm, which is considered a non-carcinogenic level, and claims completely renewed production standards in comparison with earlier acrylamide products, especially from non-European Union countries. Used strictly subcutaneously and in small volumes by experienced surgeons in a selected group of patients, polyacrylamide hydrogel has shown efficacy and a complication rate no higher than resorbable fillers in a European, multicenter, 8-year follow-up study. Removal of the gel is possible but requires a surgical setting and an experienced surgeon.64–72

Polymethylmethacrylate/Collagen Injectable Filler

In October of 2008, the U.S. Food and Drug Administration issued the first approval for a permanent dermal filler for nasolabial folds after the product had undergone multiple additional cleaning processes (Suneva Medical, Tiffin, Ohio). IQUAM emphasizes that this approval does not include substances with similar or "comparable" components from other than the mentioned company. Indications, contraindications, and experienced injection techniques are to be respected accurately.73

Gold Threads

The implantation of thin gold threads in flaccid facial cutaneous areas was developed by Caux 50 years ago. Histologically, the absence of foreign body reaction with no macrophage cells or allergic reactions following implantation of pure gold (as in eyelid correction for facial palsy, odontologic treatments) is proven. Only limited creation of reticulin fibers can be observed.

However, plication, rupture, palpability, and migration of the threads because of the mobility of the face are frequent. Efficacy has not been proven and cannot be an established standard for facial rejuvenation.74

General Recommendations Regarding Injectable Therapies

IQUAM urges governments to pass legislation to protect patients from unduly trained physicians and nonmedical personnel injecting or implanting materials for various indications. Based on experience, IQUAM states that CE marks and U.S. Food and Drug Administration approvals are required steps in establishing the safety of medical devices but are not necessarily sufficient. Postmarket surveillance revealing new adverse information should lead to reconsideration of the approval status. Therefore, it is the IQUAM members’ imperative duty to continuously monitor the short- and long-term outcomes to protect the safety of patients.

Objective medical and media reports contribute to the reassurance of patients. IQUAM will continue to provide updated information about medical devices in general and implants in particular, in addition to injectables and new technologies.

REFERENCES


