REVIEW

Breast augmentation: Part I — a review of the silicone prosthesis

MG Berry*, D.M. Davies

Institute of Cosmetic and Reconstructive Surgery, 1 Parkside, London W6 OUU, UK

Summary The present importance of breast augmentation (BA) is shown by year-on-year increases: with 8439 augmentations performed by BAAPS members in 2007[1] the UK still lags America where 307,000 were performed.[2] Having survived an almost hysterical media reaction to perceived silicone health risks in the 1990s, a growing body of evidence attests to the demonstrable benefits of BA.[3–6] Improved implant design coupled with surgical advances mean that high quality results with few complications can now be expected in the majority and a précis of progress is perhaps timely. This article forms part of a series that has been written to provide a 'state-of-the-art' review of contemporaneous BA practice.
© 2009 British Association of Plastic, Reconstructive and Aesthetic Surgeons. Published by Elsevier Ltd. All rights reserved.

History of breast augmentation

Although today synonymous with silicone-shelled prostheses, either silicone- or saline-filled, BA has seen the trial of numerous other materials. The list includes lipoma auto-transplantation,[7] paraffin injections and such esoterica as ivory and glass balls, ground rubber, ox cartilage, gutta percha, polyethylene chips, polyurethane foam sponge (Ivalon),[8] silastic rubber and liquid silicone. Autologous tissues in the form of local thoracic flaps and distant gluteal adipodermal grafts[9] were tried in the 1950s, but suboptimal results and donor scars prevented their widespread adoption. Interestingly, similar grafts have recently been revived for aesthetic contouring during cancer surgery.[10] The modern era of silicone prostheses commenced with Frank Gerow's implantation of the patient Timmie Jean Lindsey in 1962.

Despite its ubiquity and generally inert nature, silicone-based implants generated intense debate, and litigation, particularly in America. With large-scale studies repeatedly confirming the lack of association with connective tissue disease and cancer,[11–16] the pendulum has swung back in silicone's favour. Its history is, however, an interesting one: Spear's 'inside view' makes a fascinating read of 'junk science, venality and incompetence'.[17] Tebbetts holds the trenchant view that the 'silicone debate' constituted 'one of the greatest hoaxes ever perpetrated on American

* Corresponding author. Tel.: +0208 735 6060; fax: +0208 735 6061.
E-mail address: militorum@hotmail.com (MG Berry).

women by the FDA and plaintiff lawyers'.[18] However, much-needed scientific research was stimulated so we now have solid evidence on which to base and guide informed consent.

The silicone breast implant

Silicone biochemistry

Silicon is a naturally abundant element existing as obligatory oxides, of which silica (SiO_2) has numerous applications in building products, glasses and as a dessicant.[19] Humans contain 5—10 g of silicon, chiefly environmentally-acquired from silicic acid in potable water and airborne silicate dust, and studies show an important role in nail, bone and hair growth.[20] Silicone is, however, a synthetic polymer, the most common linear form being polydimethylsiloxane (PDMS; $(CH_3)_2SiO$). Silicones are ubiquitous in modern life and medicine being found in non-stick cooking utensils, feeding teats, intravenous cannulae, cardiac valves, neurological shunts and joint prostheses.[21,22]

Although silicon was first isolated in 1824, the process was prohibitively expensive and it was not until 1945 that Rochow pioneered commercial silicones. Their beneficial properties, including stability at a wide temperature range, flexibility with 'memory', water repellence (despite not being lipophilic), low toxicity and chemical reactivity, were soon apparent. There are six classes of silicone: fluid, emulsion, compound, lubricant, resin and elastomer; the latter so named for an *elast*ic return to shape after deformation and a poly*meric* structure. This property makes elastomers ideal for implant shells where the molecular structure comprises intricate, 3-dimensional cross-linked PDMS chains reinforced with 30% by weight hydrophobic amorphous silica.[19] Modern implant elastomers have a 'barrier coat' of additional phenyl (C_6H_5) or trifluoropropyl ($CF_3CH_2CH_2$) to minimise silicone transduction ('gel bleed').[23] By contrast, silicone gels are PDMS chains, lightly cross-linked through either vinyl-hydrogen bonds or as a T-shaped silicon structure. This network is expanded with silicone fluids to yield whatever cohesive or sticky composition is required[23]: currently the trend is for higher cohesion, to both limit gel travel if the elastomer fails and improve longevity. An important concept, particularly in cohesive, anatomical implants, is fracture-resistance. Gel fracture occurs when the filler is forcibly separated and if this exceeds intrinsic limits, the shape is irrevocably lost requiring replacement. Because this is most likely during insertion, longer incisions are required for anatomical prostheses. Contemporaneous implants have improved gel structures with higher fracture thresholds.

Implant evolution

Although criticised for imprecision and overlap, the 'generational' system serves as a useful guide to implant evolution (Figure 1). The historic first silicone implants from 1962 were apparently still in situ after 43 years.[8] These 'teardrop'-shaped first generation implants had a thick shell, viscous filler and a posterior Dacron patch for adherence. They felt rather firm so second generation implants with both thinner shells and filler appeared in

1972. Although more natural to the touch, they are the least durable, most prone to gel bleed, rupture and adverse capsular contracture (ACC)[24] and predominated in the 1990s' class action lawsuits. This era also introduced poly-urethane-coating to reduce ACC[25] and double-lumen implants.[26] Whilst gel bleed did reduce with the latter, complex construction increased failure rates, however, they found a role in expander-based reconstruction.[27]

Third generation implants had an additional fluorosiloxane barrier layer to combat bleed and rupture, for example, Mentor produced a quadruple-layered shell thicker anteriorly by 60% and posteriorly by 20%. Gel cohesivity increased, but these implants were firmer to the touch and required adequate soft tissue cover to minimise visibility and palpability. Following the FDA's moratorium, saline was the only filler, outwith a trial, permitted in America despite being widely accepted to have both a less natural feel and longevity: with saline not filling the shell fully, 'fold flaws' combined with the higher abrasiveness of saline, predisposed to failure.[28] Fourth generation implants had textured elastomers, based on the low rates of ACC seen with polyurethane-coating.[29] Return to an anatomical configuration was also seen during this era, championed in breast reconstruction by Maxwell.[30] The early 1990s welcomed fifth generation implants characterised by increasing gel cohesivity. Whilst all gels are to some degree cohesive in the descriptive sense of the term, cohesive implants are understood to be those that are 'form stable'. These are closer to a solid than a liquid and are formed by increasing the ratio of cross-linking so that the form is retained even without an elastomer. Not only is shape maintained longer (by resisting gravitational effects), but implant longevity should be enhanced. Explantation is also much facilitated because such gels do not disperse, even in cases of complete elastomer disruption (Figure 2), so avoiding the unpleasantly sticky removals of the older, viscous-filler prostheses. Asymmetric implants, tailored for each side, are the latest development.[31] Disadvantages of cohesive devices include their comparatively high cost and the form-stability itself, which mandates inframammary access, larger incisions and accurate selection. Implant rupture may be harder to diagnose, but the long-term

Figure 1   Image of cohesive 'form-stable' silicone implant demonstrating the difficulty in forcing the gel out of the elastomer even when completely disrupted.

consequences are as yet unknown. Being so recent, long-term follow up data is not available, but early results for both patient satisfaction and ACC are encouraging,[32] particularly by those who have applied analytical surgical methodology.[6,33]

Polyurethane-coating

Although withdrawn in 1991, polyurethane implants are staging a comeback and, in fact, predated silicone implants appearing as they did in the 1950s. Concerns about disintegration of the external polyurethane coating[34] had been mounting, but the final nail in the coffin were animal studies linking its breakdown product, 2-toluene diamine (TDA), to carcinogenesis.[23] It is now accepted, however, that any human risk is negligible given that cancer-prone animals were subjected to supra-physiological TDA concentrations.[35] There are now many tens of thousands of patients with polyurethane-coated prostheses in situ for

over a decade without any concerns. Polyurethane itself is probably relatively stable as shown by a recent report of a solid polyurethane sponge augmentation that ran into difficulties unilaterally, only after 41 years.[8] Early studies showed impressively low ACC[25,36] explained by polyurethane eliciting a vigorous, vascular foreign body reaction that, by persisting, prevented fibroblasts from laying down collagen in a continuous, plane thereby neutralising the circular vector forces that produced ACC. The lack of durability of the external coat led to a delayed peak of ACC, for example 10% at 4 years, but 25% by 10 years, as the prevalence returned to that of contemporaneous implants.[37] There were also reports of difficulties with explantation resulting from extensive host ingrowth.[38] The associated, generally transient, skin rash may have been an allergic reaction to the adhesive used for affixing the polyurethane coat. At present, improved polyurethane-coated prostheses are being marketed for revisional surgery in ACC, based on a recent prospective study showing that
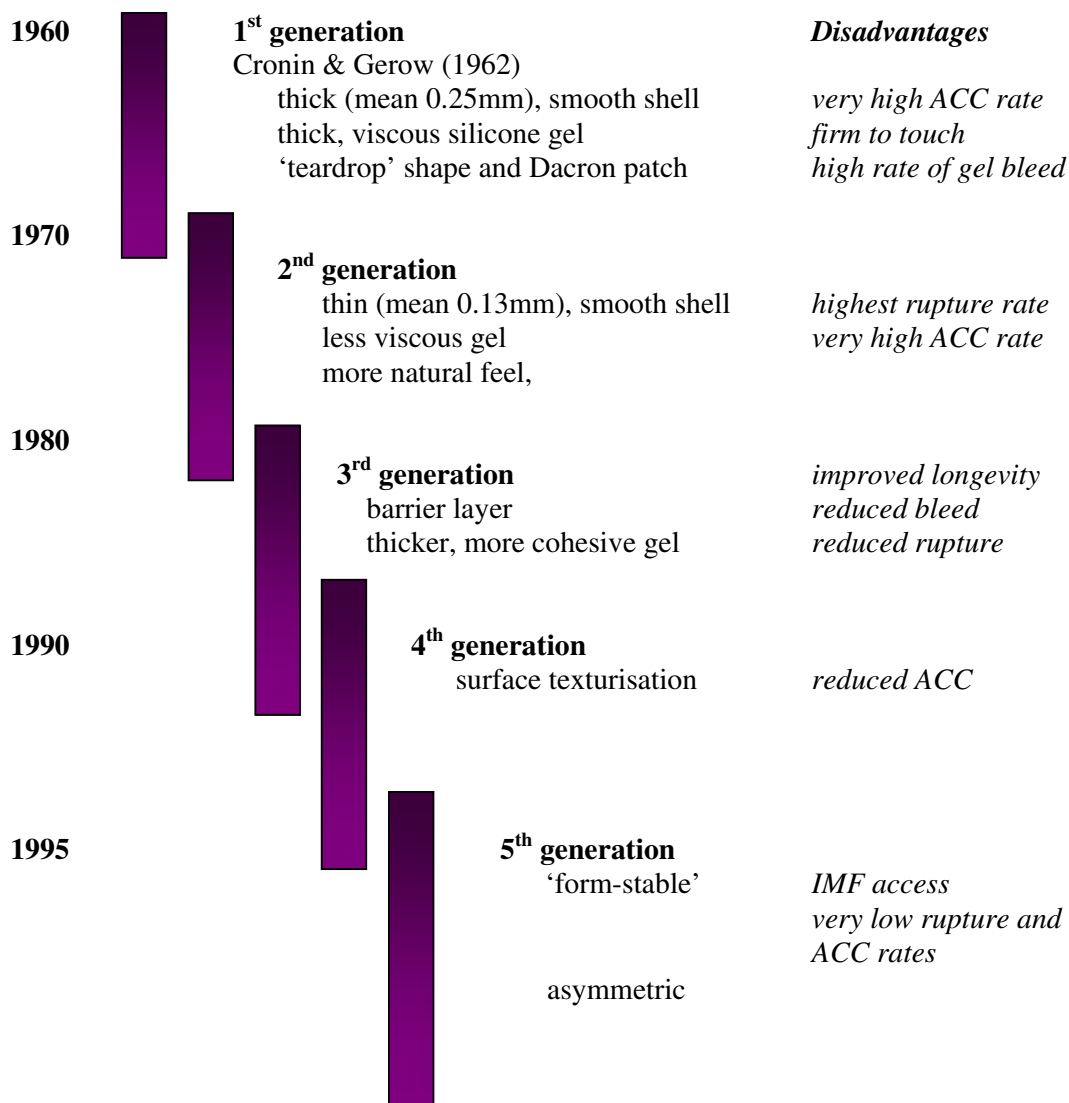
Year	Generation	Disadvantages

1960	**1st generation**
	Cronin & Gerow (1962)
	  thick (mean 0.25mm), smooth shell
	  thick, viscous silicone gel
	  'teardrop' shape and Dacron patch
		Disadvantages
		
		very high ACC rate
		firm to touch
		high rate of gel bleed

1970	**2nd generation**
	  thin (mean 0.13mm), smooth shell
	  less viscous gel
	  more natural feel,
		
		highest rupture rate
		very high ACC rate

1980	**3rd generation**
	  barrier layer
	  thicker, more cohesive gel
		improved longevity
		reduced bleed
		reduced rupture

1990	**4th generation** surface texturisation	*reduced ACC*

1995	**5th generation**
	  'form-stable'
	
	  asymmetric
		IMF access
		very low rupture and
		ACC rates

Figure 2   Five generations of silicone gel mammary prostheses (after Independent Review Group). ACC — adverse capsular contracture; IMF — infra-mammary fold.

dramatically lower ACC rates persist beyond 10 years of implantation.[39]

Silicone alternatives

There have been several alternative fillers in the 1990s when silicone-phobia peaked: unfortunately, these products were rushed to the market after cursory pre-clinical trials. Three were based on hydrogels, another on soya bean oil. Hydrogels are polymeric macromolecules that retain water without dissolution. Hydroxypropylcellulose, formed the basis of the Polyimplant Prosthesis™ (PIP; Clover Leaf Products, UK) and was implanted into 4000 UK women. The Misti Gold prosthesis (Bioplasty Inc., Mn., USA), based on synthetic low molecular weight polyvinylpyrrolidone, was trialled in 1990–1, but combined disappointing results with high cost.[40] Novagold™ comprised the synthetic polymer polyvinylpyrrolidone (povidone) and guar gum. Povidone has seen service for plasma expansion, biomedical coating and the iodine carrier in Betadine. Guar gum, from *Cyamopsis tetragonoloba*, is a foodstuff stabiliser-thickener and was added to povidone for the same reason. A recent review of patients with Novagold™ prostheses confirmed a high rupture rate (double that of saline) due to oncotic swelling.[41] Although non-toxic, these fillers induce a vigorous subcutaneous inflammatory reaction and explantation is recommended when symptomatic.

Simultaneously, triglycerides were being promoted for improved radiolucency and biocompatibility,[42] although a 5.5% bleed rate within 6 months was explained away by the measuring process.[28] The Trilucent (LipoMatrix, Neuchâtel, Switzerland) implant, named from *tri*glyceride and radio*lucent*, was implanted in almost 5000 women in the UK between 1995 and 1999. It contained refined USP medical grade soyabean oil within a silicone elastomer, which had a metallic data transponder that was soon found to somewhat limit magnetic resonance imaging (MRI). Kirkpatrick et al's study of soyabean oil, particularly its peroxidation to genotoxic degradation products observed that, limited, pre-market trials were undertaken in America, yet the device was never used there.[43] They were voluntarily withdrawn in March 1999 after adverse reports[44] and the Medical Devices Agency made a formal recommendation for removal in June 2000. Explantation studies showed variable satisfaction and problems including shell fragility, lipid absorption, firm adherence to thick vascular capsules, delamination and a bleed rate of 34%.[44,45]

Until recently the sole option in the US, the first saline-filled implant was developed by the Frenchman Arion, however, it is worth noting that these too are silicone-shelled. Although one might expect easier mammography, in fact, their radiolucency is, due to a high atomic number, little different to silicone. Furthermore, they suffer from more visible and palpable rippling so are not ideal for thin patients.[4] Finally, their consistency is said by some to be firmer than modern gels, they have the potential for 'fold flaw' disruption and complete deflation, although saline is, of course, entirely safe and will simply be absorbed.

To avoid silicone altogether biological substances such as hyaluronic acid (HA), a major constituent of extracellular matrices, have been trialled. Although more radiolucent, and softer than silicone,[46] HA is naturally degraded thus is non-permanent and rather expensive.[47] An improved volume restoration-factor of the HA Macrolane™ (Q-Med AB) has shown promise for so-called 'minimally invasive' BA.[48] but the costs of the initial, and necessary supplementary injections, are similar to that for silicone augmentation, which is permanent.

Contemporaneously, fat transfer is increasingly popular and Coleman recently reported impressive results in primary BA grafting a remarkable mean of 277 cc fat per breast.[49] That fat transfer is de rigeur is evidenced by the Canniesburn group's BAPRAS presentation[50] and an accredited reconstructive and aesthetic seminar.[51] That autografted fat improves overlying skin and soft tissue quality[49] and, via adipose-derived stem cells, heals radio-necrotic ulceration[52] suggests a potentially useful future role especially in revision surgery. Non-surgical alternatives have also been explored. Suction devices first used in the 1920s were revived recently as the BRAVA system, which functions through tension-induced neo-tissue generation; similar to tissue expansion and distraction osteogenesis.[53] Despite some enthusiasm, results have not been replicated chiefly for functional difficulties and compliance: most finding the recommended 10 h daily for 10 weeks onerous given the modest and transient results.[54] There is also the potential for aggravating ptosis. Unsurprisingly, the internet and non-medical literature abound with herbal and homeopathic remedies, but none have as yet been subjected to any degree of scientific validation.[55]

Implant regulations

As an implantable medical device, breast prostheses are subject to a number of regulations including the 1993 European Medical Devices Directive[56] and 2002's national UK law.[57] They require notification of certain adverse incidents, under the 'vigilance system', to both protect the patient and reduce similar incidents occurring elsewhere. Importantly, procedures must exist to both systematically audit post-production experience and implement corrective action such as a product recall. Notifiable incidents include device deterioration or failure and poor instructions resulting in improper use. Interestingly, delayed ACC is specified, presumably to avoid a repeat of the polyurethane issue.

There are four classes of medical devices according to risk: low (Class I), moderate (Classes IIa/b) and high (Class III). In 2003 breast implants were reclassified level III in order to bring all European implants in line with the UK.[58] CE (Conformité Européene) marking is a manufacturer's declaration that the product complies with the health, safety and environmental requirements of the relevant Product Directive. It is a mark of quality assurance and allows free trade throughout Europe, though is not required for export.

The UK Breast Implant Registry, or in its earlier guise the National Breast Implant Registry, was established in 1993. Unfortunately, it was disbanded in March 2006 following independent audit that found it unable to produce scientifically apposite results due to poor participation. Registration was perhaps hampered by the voluntary nature and requirement for patient consent.

Silicone safety aspects

Teratogenicity

Despite reports of rashes and oesophageal dysmotility in children of silicone-augmented mothers, the IRG found no evidence that exposure was greater from maternal than environmental silicone.[22] Although capsule and breast levels are elevated, cadaveric silicon levels remote from the breast in augmented women are equivalent to non-augmentees indicating ubiquitous environmental exposure.[21] A detailed study established that silicon (used as a proxy for silicone, which is not directly assayable) was found in equivalent levels in the milk of breastfeeding women with and without silicone implants.[59] Furthermore, much higher levels of silicon were found in cow's milk and infant formulae, in excess of 10- and 90-fold respectively.

Breast cancer

The role of silicone implants in breast cancer has been subject to much debate and many of the keynote publications are common to connective tissue diseases (CTDs),[14,15,22] but cancer brings the further issue of screening and surveillance. Both silicone and saline, with similar radiodensities, may interfere with the sensitivity of imaging, so specialised views are required. Eklund added a lateral view and displacement techniques to move the implant posteriorly.[60] Logically, submuscular implants allow for better visualisation[15] and ACC less. For both stage at diagnosis and subsequent prognosis there is no evidence of a difference[61] and, indeed, some have shown smaller tumours on presentation in augmentees with similar axillary node involvement.[61,62] That tumours are more often diagnosed following palpation yet are no larger, more advanced or with poorer prognosis suggests that augmentation renders tumours more obvious[39] and/or that augmentees are more breast-aware. Interestingly, evidence exists for a trend towards a lower rate of breast cancer in women with implants.[16,35] Whilst the reason for a lower prevalence is unknown implants themselves may possess an anticarcinogenic effect, either as a barrier to spread or via pressure-mediated tumour blood flow inhibition,[63] or through a collateral effect of the foreign body reaction.[35] It may simply reflect the smaller breast parenchyma a priori. A recent review reiterated that augmentees: i) are more likely to present with palpable tumours, ii) have a similar incidence of nodal metastasis and iii) have no worse a prognosis.[64] As to cancer management, sentinel node biopsy is usually possible, unless implantation was trans-axillary and, although more challenging, acceptable results are possible with therapeutic mammaplasty techniques.[65]

Whilst recent long-term studies confirm the lower incidence of breast cancer[16] there is some evidence of increased bronchopulmonary and vulvar carcinoma, at present attributed to lifestyle factors. It is becoming clear that BA patients form a population subset, which is thinner, younger at first pregnancy and multiparous. Smoking seems to be a risk factor in European, but not American patients.[66,67] There may also be an increased risk of suicide, drug and alcohol dependence.[68]

Autoimmune and connective tissue disease

The first documented association with several autoimmune conditions including systemic lupus erythematosus, scleroderma, dermatomyositis, Sjogren's syndrome and rheumatoid arthritis appeared in 1964 following silicone injection mammaplasty.[21] In Stern vs. Dow Corning, the jury adjudged autoimmune disease to result from silicone prostheses based on limited medical evidence[69] and in 1991, a \$5.4 m award followed the demonstration of intra-immune system silicone in Toole vs. Baxter. In 1992, the FDA imposed a voluntary moratorium, which became a de facto ban, of silicone-filled prostheses for anything other than reconstruction: the implant shells, of course, remained silicone. 1994 saw the first large-scale report, which found no increase in 12 common CTDs.[11] The American College of Rheumatology's 1995 statement concluded the evidence to be 'compelling' that silicone implants exposed patients to no demonstrable risk for CTDs.[70] The Harvard Nurses' Study of 14-year follow up showed a relative risk of 0.6 for any and 0.3 for silicone gel implants: importantly this data was collected prior to widespread media coverage.[12] By 1999, the Institute of Medicine-National Academy of Sciences confirmed the absence of causal association with immunological or systemic diseases.[14] Whilst the FDA acknowledged these conclusions, they imposed stringent conditions that device failure was to be tested and rates known prior to restoring vending privileges. The UK view was more measured and the 1998 Independent Review Group publication remains a thorough and concise resumé[22] and one which all patients should be encouraged to read. The IRG last met in April 2004 and was satisfied that silicone breast implants posed no greater health risk than other implants. A Swedish study, with nationwide registration and relative American media isolation, found a relative risk of 0.8% for augmentees.[71] The most comprehensive meta-analysis to date confirmed lower relative risks for silicone-filled implants[13] and a recent review reiterated the lack of association over a 24 year period.[72] The FDA finally approved silicone gel-filled breast prostheses for augmentation in December 2006.

Implant rupture

The excellent summary of complications by Iwuagwu remains apposite in its breadth,[73] even if the frequencies have diminished of late.[1] Recent Scandinavian population reviews have showed that most early complications, are clinically insignificant[74,75] and super-specialists indicate a 0% reoperation rate at 3 years.[33] The chief concerns necessitating additional surgery remain ACC and rupture; the former will be addressed in a future article.

Despite significant advances, implants are mechanical devices so do not have an indefinite life in vivo and elastomer integrity declines with time, possibly as a consequence of lipid infiltration.[76] The difficulty in counselling lies with risk quantification as the longest follow up data relates to the oldest, and therefore least durable, implants. Failure is undoubtedly multi-factorial, but causes include per-implantation damage, thoracic trauma, mammography and closed capsulotomy.[77] Chronic stress-loading with

subpectoral placement may also contribute,[24] but the majority appear idiopathic. Implant rupture may be intra-capsular, where external appearance is dictated by the capsule, or extra-capsular where silicone breaches. Saline-filled implants, of course, herald their failure with deflation.

With clinical detection by experienced Plastic Surgeons less than 30% accurate,[78] the 91% specificity of MRI makes it the investigation of choice for suspected rupture.[79] Whilst the FDA recommend MRI 3 years post-implantation and biennially thereafter, outwith the US it is reserved for suspected rupture. Features include a 'doughy' consistency, calcification, granulomata and pain.[78] With 3rd/4th generation implants the rupture risk is estimated at 8–15% for the first decade: put another way there is a 95% probability of an implant being intact at 5 and 83–85% at 10 years.[80] The most recent cohesive anatomical devices are showing encouraging initial rates of 0% at 3[32] and ≤1% at 6 years.[6]

Rupture ranges from focal (pin-hole), through a visible tear to major shell disruption and is probably progressive. The three characteristic MRI features are: 'subcapsular line' — an interface between shell and capsule caused by a small quantity of leaked gel. Further extravasation produces the 'inverted teardrop' as silicone is trapped within elastomeric folds. Major disruption, where the shell collapses onto itself is seen as the 'linguine' sign.[81] Although intra-capsular can progress to extra-capsular rupture,[82] complications tend to be limited loco-regionally.[81] At present there is no consensus as to the long-term consequences of interstitial silicone.

Although useful, imaging is imperfect and several explantation studies have been published. Robinson et al, found 71.3% of 300 explantees had time-dependant disruption of one or both implants[83]: 75% had, however, undergone closed capsulotomy and elective removal was recommended. Another retrospective series, of 478, found rupture not to be temporally-dependent.[24] A prospective series of 38 explantations for health concerns rather than suspected rupture concluded that those with silicone implants noted more bodily pain, however, were happier with their appearance and 50% were re-augmented within 2 years.[84] For advice to patients, Holmich's study of sequential MRIs concluded that rupture was harmless in the majority. Whilst there was a 1-in-10 risk of progression, either intra- to extra-capsular or extra-capsular extension, the majority could be followed expectantly.[85]

Summary

Breast augmentation remains an increasingly popular option today where the idealised female physique has morphed from the curvaceous Botticellean to one increasingly thin and androgynous, but with prominent breasts. From humble, and perhaps somewhat disorganised, beginnings the silicone gel prosthesis has now been accorded an, almost, clean bill of health. Whilst the dark years of the 1990s make for interesting reading, they at least catalysed a body of scientific evidence for surgeons and patients alike. It also demonstrates the requirement for science to be sufficiently robust to withstand highjack and subversion

from a sensationalist, and not always patient-centred media, and for all parties to show patience with pioneers of novel techniques. The knee-jerk, anti-silicone foray into hydrogel and soya bean fillers was readily accepted due to the pervasive 'junk science' furore, but may now be regarded as ill-considered. Certain legal teams enriched themselves massively at the expense of ill-prepared organisations, such as Dow Corning, and one can only wonder at the outcome of a challenge against such a plaintiff counsel from a patient forced into accepting a Trilucent implant. BA is a safe, well-accepted technique, which can be undertaken with ever-less frequent complications thanks to continued advances in both technique and implant design.

Conflict of interest

Neither author has a conflict of interest or funding to disclose.

References

1. Also Avaliable at: http://www.baaps.org.uk/content/view/404/62 [accessed 10th June 2009].
2. Also Avaliable at: http://www.plasticsurgery.org/Media/stats/2008 [accessed 10th June 2009].
3. Park AJ, Chetty U, Watson ACH. Patient satisfaction following insertion of silicone breast implants. *Br J Plast Surg* 1996;**49**:515–8.
4. Hedén P, Jernbeck J, Hober M. Breast augmentation with anatomical cohesive gel implants. *Clin Plast Surg* 2001;**28**:531–52.
5. Cash TF, Duel LA, Perkins LL. Women's psychological outcomes of breast augmentation with silicone gel-filled implants: a 2-year prospective study. *Plast Reconstr Surg* 2002;**109**:2112–21.
6. Hedén P, Boné B, Murphy DK, et al. Style 410 cohesive silicone breast implants: safety and effectiveness at 5 to 9 years after implantation. *Plast Reconstr Surg* 2006;**118**:1281–7.
7. Czerny V. Plastischer ersatz der brustdruse durch ein lipom. *Zentralbl Chir* 1895;**27**:72.
8. Nahabedian M. Explantation of 41-year-old implants following primary breast augmentation. *Ann Plast Surg* 2007;**58**:91–4.
9. Watson J. Some observations on free fat grafts: with reference to their use in mammaplasty. *Br J Plast Surg* 1959;**12**:263–74.
10. Kijima Y, Yoshinaka H, Owaki T, et al. Early experience of immediate reconstruction using autologous free dermal fat graft after breast conservational surgery. *J Plast Reconstr Aesthet Surg* 2007;**60**:495–502.
11. Gabriel SE, O'Fallon WM, Kurland LT, et al. Risk of connective-tissue diseases and other disorders after breast implantation. *N Engl J Med* 1994;**330**:1697–702.
12. Sanchez-Guerrero J, Colditz GA, Karlson EW, et al. Silicone breast implants and the risk of connective-tissue diseases and symptoms. *N Engl J Med* 1995;**332**:1666–70.
13. Janowsky EC, Kupper LL, Hulka BS. Meta-analysis of the relation between silicone breast implants and the risk of connective-tissue diseases. *N Engl J Med* 2000;**342**:781–90.
14. Institute of Medicine. *Safety of silicone breast implants*. Washington, D.C.: National Academy Press; 1999.
15. Muzaffar AR, Rohrich RJ. The silicone gel-filled breast implant controversy: an update. *Plast Reconstr Surg* 2001;**109**:742–7.
16. Deapen DM, Hirsch EM, Brody GS. Cancer risk among Los Angeles women with cosmetic breast implants. *Plast Reconstr Surg* 2007;**119**:1987–92.
17. Spear S. The breast implant story. *Ann Plast Surg* 2006;**56**:573–83.

18. Tebbetts JB, Tebbetts TB. *The best breast*. 1st ed. Dallas: CosmetXpertise; 1999.

19. LeVier RR, Harrison MC, Cook RR, et al. What is silicone? *Plast Reconstr Surg* 1993;**92**:163—7.

20. Byczkowski S, Wrzeniowska K. Studies on the physiological hair silicon content in men. *Toxicology* 1975;**5**:123—4.

21. Evans GR, Netscher DT, Schusterman MA, et al. Silicon tissue assays: a comparison of nonaugmented cadaveric and augmented patient levels. *Plast Reconstr Surg* 1996;**97**:1207—14.

22. Independent Review Group (IRG). Silicone gel breast implants: the report of the Independent Review Group. July 1998.

23. Dunn KW, Hall PN, Khoo CT. Breast implant materials: sense and safety. *Br J Plast Surg* 1992;**45**:315—21.

24. Collis N, Sharpe DT. Silicone gel-filled breast implant integrity: a retrospective review of 478 consecutively explanted implants. *Plast Reconstr Surg* 2000;**105**:1979—85.

25. Herman S. The Même implant. *Plast Reconstr Surg* 1984;**73**:411—4.

26. Radovan C. Breast reconstruction after mastectomy using the temporary expander. *Plast Reconstr Surg* 1982;**69**:195—208.

27. Becker H. Breast reconstruction using an inflatable breast implant with detachable reservoir. *Plast Reconstr Surg* 1984;**73**:678—83.

28. Young VL, Lund H, Ueko K, et al. Bleed of and biologic response to triglyceride filler used in radiolucent implants. *Plast Reconstr Surg* 1996;**97**:1179—93.

29. Brand KG. Polyurethane-coated silicone implants and the question of capsular contracture. *Plast Reconstr Surg* 1984;**73**:498.

30. Maxwell GP, Falcone PA. Eighty-four consecutive breast reconstructions using a textured silicone tissue expander. *Plast Reconstr Surg* 1992;**89**:1022—34.

31. Fitoussi AD, Couturaud B. Evaluation des prothèses asymétriques dans la chirurgie mammaire d'augmentation. *Ann Chir Plast Esthet* 2005;**50**:517—23.

32. Fruhstorfer BH, Hodgson ELB, Malata CM. Early experience with an anatomical soft cohesive silicone gel prosthesis in cosmetic and reconstructive breast implant surgery. *Ann Plast Surg* 2004;**53**:536—42.

33. Tebbetts JB. Achieving a zero percent reoperation rate at 3 years in a 50-consecutive-case augmentation mammaplasty premarket appraisal study. *Plast Reconstr Surg* 2006;**118**:1453—7.

34. Sinclair TM, Kerrigan CL, Buntic R. Biodegradation of the polyurethane foam covering of breast implants. *Plast Reconstr Surg* 1993;**92**:1003—13.

35. Deapen DM, Bernstein L, Brody GS. Are breast implants anti-carcinogenic? a 14-year follow-up of the Los Angeles study. *Plast Reconstr Surg* 1997;**99**:1346—53.

36. Ashley FL. A new type of breast prosthesis: preliminary report. *Plast Reconstr Surg* 1970;**45**:421—4.

37. Collis N, Coleman DJ, Foo ITH, et al. Ten-year review of a prospective randomized controlled trial of textured versus smooth subglandular silicone gel breast implants. *Plast Reconstr Surg* 2000;**106**:786—90.

38. Brody GS. Discussion. *Plast Reconstr Surg* 1984;**73**:420—1.

39. Handel N, Silverstein MJ. Breast cancer diagnosis and prognosis in augmented women. *Plast Reconstr Surg* 2006;**118**:587—93.

40. Laing JHE, Sanders R. The Misti Gold bio-oncotic gel filled prosthesis: an acceptable alternative to silicone? *Br J Plast Surg* 1993;**46**:240—2.

41. Hardwicke J, Gaze NR, Laitung JKG. A retrospective audit of Novagold™ 'hydrogel' breast implants. *J Plast Reconstr Aesthet Surg* 2007;**60**:1313—6.

42. Young VL, Lund H, Destouet J, et al. Biocompatibility of radiolucent breast implants. *Plast Reconstr Surg* 1991;**88**:462—74.

43. Kirkpatrick WNA, Jones BM. The history of Trilucent implants, and a chemical analysis of the triglyceride filler in 51 consecutively removed Trilucent breast prosthesis. *Br J Plast Surg* 2002;**55**:479—88.

44. Davies DM, Kirkpatrick WNA. Lipid emulsification after implant rupture. *Br J Plast Surg* 1999;**52**:238.

45. Rizkalla M, Webb J, Chuo CB, et al. Experience of explantation of Trilucent breast implants. *Br J Plast Surg* 2002;**55**:117—9.

46. Lin K, Bartlett SP, Matsuo K, et al. Hyaluronic acid-filled mammary implants: an experimental study. *Plast Reconstr Surg* 1994;**94**:306—15.

47. Price RD, Berry MG, Navsaria HA. Hyaluronic acid: the scientific and clinical evidence. *J Plast Reconstr Aesthet Surg* 2007;**60**:1110—9.

48. Hedén P, Sellman G, von Wachenfeldt, et al. Body shaping and volume restoration: the role of hyaluronic acid. *Aesthetic Plast Surg* 2009;**33**:274—82.

49. Coleman SR. Fat grafting to the breast revisited: safety and efficacy. *Plast Reconstr Surg* 2007;**119**:775—85.

50. Mandal A, Weiler-Mithoff E. Lipomodelling of the reconstructed breast - the Canniesburn learning curve experience. British Association of Plastic Reconstructive and Reconstructive Surgery Summer Meeting. Deauville, France. July 2007.

51. Anon. Advanced plastic surgery of the breast: vascularised fat transfer and lipo-modelling in reconstructive and aesthetic breast surgery. Birmingham, October 2007.

52. Rigotti G, Marchi A, Galiè M, et al. Clinical treatment of radiotherapy tissue damages by lipoaspirate transplant: a healing process mediated by adipose-derived stem cells. *Plast Reconstr Surg* 2007;**119**:1409—22.

53. Khouri RK, Schlenz I, Murphy BJ, et al. Non surgical enlargement using an external soft-tissue expansion system. *Plast Reconstr Surg* 2000;**105**:2500—12.

54. Smith C. Initial experience with the BRAVA nonsurgical system of breast enhancement. *Plast Reconstr Surg* 2002;**110**:1593—5.

55. Chalfoun C, McDaniel C, Motarjem P, et al. Breast-enhancing pills: myth and reality. *Plast Reconstr Surg* 2004;**114**:1330—3.

56. Council of the European Communities. Council directive 93/42/EEC of June 1993 concerning medical devices. OJ L169:1—43. 1993.

57. *Great Britain. The Medical Devices Regulations 2002*. SI 2002 No. 618. London: HMSO, ISBN 0110423178; 2002.

58. Avaliable at: http://www.dh.gov.uk/en/Publicationsandstatistics/Pressreleases /DH_4047362. Published 25th July 2003.

59. Semple J, Lugowski SJ, Baines CJ, et al. Breast milk contamination and silicone implants: preliminary results using silicon as a proxy measurement for silicone. *Plast Reconstr Surg* 1998;**102**:528—33.

60. Eklund GW, Busby RC, Miller SH, et al. Improved imaging of the augmented breast. *Am J Roentgenol* 1988;**151**:469—73.

61. Clark 3rd CP, Peters GN, O'Brien KM. Cancer in the augmented breast. Diagnosis and prognosis. *Cancer* 1993;**72**:2170—4.

62. Birdsell DC, Jenkins H, Berkel H. Breast cancer diagnosis and survival in women with and without breast implants. *Plast Reconstr Surg* 1993;**92**:795—800.

63. Ramasastry SS, Weinstein LW, Zerbe A, et al. *Plast Reconstr Surg* 1991;**87**:1—7.

64. McIntosh SA, Horgan K. Breast cancer following augmentation mammoplasty — a review of its impact on prognosis and management. *J Plast Reconstr Aesthet Surg* 2007;**60**:1127—35.

65. McCulley SJ, Macmillan RD. Planning and use of therapeutic mammplasty — nottingham approach. *Br J Plast Surg* 2005;**58**:889—901.

66. Kjoller K, Hölmich LR, Fryzek JP, et al. Characteristics of women with cosmetic breast implants compared with women with other types of cosmetic surgery and population-based controls in Denmark. *Ann Plast Surg* 2003;**50**:6—12.

67. Brinton LA, Brown L, Colton T, et al. Characteristics of a population of women with breast implants compared with women

seeking other types of plastic surgery. *Plast Reconstr Surg* 2000;**105**:919–27.

68. Lipworth L, Nyren O, Ye W, et al. Excess mortality from suicide and other external causes of death among women with cosmetic breast implants. *Ann Plast Surg* 2007;**59**:119–23.

69. van Nunen SA, Gatenby PA, Basten A. Post-mammoplasty connective tissue disease. *Arthritis Rheum* 1982;**25**:694–7.

70. American College of Rheumatology. Statement on Silicone Breast Implants. Atlanta, GA., October 24, 1995.

71. Nyren O, Yin L, Josefsson S, et al. Risk of connective tissue disease and related disorders among women with breast implants: a nation-wide retrospective cohort study in Sweden. *Br Med J* 1998;**316**:417–22.

72. Fryzek JP, Holmich L, McLaughlin JK, et al. A nationwide study of connective tissue disease and other rheumatic conditions among danish women with long-term breast implantation. *Ann Epidemiol* 2007;**17**:374–9.

73. Iwuagwu FC, Frame JD. Silicone breast implants: complications. *Br J Plast Surg* 1997;**50**:632–6.

74. Henriksen TF, Hölmich L, Fryzek JP, et al. Incidence and severity of short-term complication s after breast augmentation: results from a nationwide breast implant registry. *Ann Plast Surg* 2003;**51**:531–9.

75. Kulmala I, McLaughlin JK, Pakkanen M, et al. Local complications after cosmetic breast implant surgery in Finland. *Ann Plast Surg* 2004;**53**:413–9.

76. Adams Jr WP, Robinson JB, Rohrich RJ. Lipid infiltration as a possible biologic cause of silicone gel breast implant aging. *Plast Reconstr Surg* 1998;**101**:64–8.

77. Goin JM. High-pressure injection of silicone gel into an axilla – a complication of closed compression capsulotomy of the breast. *Plast Reconstr Surg* 1978;**62**:891–5.

78. Hölmich LR, Fryzek JP, Kjoller K, et al. The diagnosis of silicone breast-implant rupture: clinical findings compared with findings at magnetic resonance imaging. *Ann Plast Surg* 2005;**54**:583–9.

79. Cher DJ, Conwell JA, Mandel JS. MRI for detecting silicone breast implant rupture: meta-analysis and implications. *Ann Plast Surg* 2001;**47**:367–80.

80. Hölmich LR, Friis S, Fryzek JP, et al. Incidence of silicone breast implant rupture. *Arch Surg* 2003;**138**:801–6.

81. Brown LS, Silverman BG, Wendie A. Rupture of silicone-gel breast implants: causes, sequelae and diagnosis. *Lancet* 1997;**350**:1531–7.

82. Malyon AD, Dunn R, Weiler-Mithoff EM. Expanding silicone granuloma. *Br J Plast Surg* 2001;**54**:257–9.

83. Robinson Jr OG, Bradley EL, Wilson DS. Analysis of explanted silicone implants: a report of 300 patients. *Ann Plast Surg* 1995;**34**:1–6.

84. Rohrich RJ, Kenkel JM, Adams WP, et al. A prospective analysis of patients undergoing silicone breast implant explantation. *Plast Reconstr Surg* 2000;**105**:2529–37.

85. Hölmich LR, Vejborg IM, Conrad C, et al. Untreated silicone breast implant rupture. *Plast Reconstr Surg* 2004;**114**:204–14.