Examination of Poly Implant Prothèse (PIP) silicone breast implant retrieval study by Swarts *et al* (2012)

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Introduction

The scandal of allegedly sub-standard mammary prostheses made by the French Manufacturer, Poly Implant Prothèse (PIP) continues to attract considerable attention. Criticisms or inadequacies alleged in the product do not yet appear to withstand the rigours of impartial, objective, scientific, epidemiological and balanced study by the regulators concerned; further, insufficient, truly independent scientific examination of the products has been available to date (Atchia, 2012 a and b). A few studies examining explanted units of the product are now emerging. Although those published so far are not part of controlled, observational design and are certainly statistically un-determinative, they do provide growing information on the behaviour of such devices in the body.

This article examines one of the most recent retrieval studies critically, in an attempt to evaluate its findings scientifically.

Swarts *et al* (2012) examined n=19 ruptured PIP breast implants explanted from n=27 patients to evaluate possible changes in properties of the device possibly occurring during residence in the body of the subjects.

Tests were limited to mechanical properties specified by ISO 14607, certain dimensions and comparison with virgin, un-implanted controls. The authors considered application of ISO 14607 to assess explanted units was reasonable, however, it is argued that premiss is specious given the various deficiencies in the methods and range of tests specified therein. Nevertheless, n=19 ruptured, explanted and n=2 virgin, un-implanted PIP silicone pre-filled breast implants, were tested. Data on controls were combined with those from tests on n=15 performed by TGA. The following tests were performed:

- Tensile
  - load to failure (ISO 14607 Annex B)
  - elongation (ISO 14607 Annex B1.2)
  - tensile set (ISO 14607 Annex B1.3)
  - join strength (ISO 14607 Annex B2.2)
  - seam strength
  - seal strength
- Compression
  - Impact resistance (ISO 14607 Annex E.2)
  - Static rupture (ISO 14607 Annex E.3)
- Gel cohesion (ISO 14607 Annex D)

- Molecular weight analysis (only n=2 explants)
  - Gel permeation chromatography

N=5 dumb-bell shaped specimens were excided from the shell of each test and control implant according to ISO 37, plus n=2 from the welded patch (of each test and control implant).

Additionally, formalin-preserved samples of breast tissue supplied by the referring surgeon were submitted to tissue silicon analysis by inductively coupled plasma atomic emission spectroscopy.

Results are reproduced in Tables 1-3.

Table 1. Tensile test results (from Swarts *et al*, 2012)

PIP Samples	Elongation (Annex B1.2)	Tensile Strength (Annex B1.3)	Patch/seams (Annex B2.2)
New textured (control 1, n=1)	650% (pass)	1.5% (pass)	Pass
New textured (TGA, n=8)*	546%-619% (all passed)		
New smooth (control 2, n=1)	840% (pass)	0.7% (pass)	Pass
New smooth (TGA, n=7)*	513%-666% (all passed)		
Ruptured (n=19)	500%-760% (all passed)	0.1% - 2.5% (all passed)	All passed

Note: *TGA results (in Swarts *et al*)

Table 2. Gel cohesion and compression test results (ISO 14607) (from Swarts *et al*, 2012)

Gel Cohesion (Annex D) (n=19)	Impact Resistance (Annex E.2) (n=18)	Static Rupture (Annex E.3) (n=25)
1 failed	2 failed Rupture passed through ID markings in one sample. All failed samples with thickness variability	• 5 samples ruptured at ≤ 2150N • Average rupture value = 5493N • Highest value = 9500N • Lowest value = 300N Rupture passed through ID markings in one sample. All failed samples showed thickness variability

Table 3. Details of silicone gel and shell of ruptured PIP devices & Table 4. Rupture characteristics of explanted PIP devices

Explant	Site	Time in situ (yr)	Time since production (yr)	Volume (cc)	Gel adhesion	Gel colouration	Former markings	Shell layers ^	Features at rupture site	Rupture size	Rupture location	Rupture appearance
1	Right	5.4	7	350	n	Light yellow	No	Multi	Rupture along ID marks and patch	Large	Anterior & posterior	Radial
2	Right	2.8	5	435	a	Yellow	Yes	Multi	Rupture along patch	Large	Anterior & posterior	Radial
3	Right	6.0	6.8	350	n	Yellow	Yes	Multi	Rupture along patch	Large	Anterior & posterior	Radial & tangential
4	Right	6.5	7	290	a	Yellow	Yes	Multi	No distinct features	Large	posterior	Radial
5	Right	4.4	4.8	210	n	Yellow	Yes	Single	Rupture along ID marks and patch	Large	Anterior & posterior	Radial
6	Left	6.5	7	290	n	Light yellow	Yes	Multi	Rupture along patch	Small	Anterior & posterior	Tangential
7	Right	5.8	Unknown	365	a	Light yellow	Yes	Multi	Rupture along ID marks and patch	Small	posterior	Small crack
8	Left	5.3	5.5	330	n	Yellow	Yes	Multi	No distinct features	Small	Anterior & posterior	u shaped

Explant	Site	Time in situ (yr)	Time since production (yr)	Volume (cc)	Gel adhesion	Gel colouration	Former markings	Shell layers ^	Features at rupture site	Rupture size	Rupture location	Rupture appearance
9	Right	5.8	Unknown	310	n	Yellow	Yes	Multi	No distinct features	Large	Anterior & posterior	Tangential
10	Right	6.6	7	290	a	Yellow	Yes	Multi	No distinct features	Small	Anterior	Circumferential
11	Left	4.2	4.4	310	n	Light yellow	Yes	Single	Scratch marks	Small	anterior	Circumferential
12	Right	4.2	4.4	310	a	Light yellow	Yes	Single	No distinct features	Small	Posterior	u shaped
13	Right	6.2	7	290	n	Light yellow	No	Multi	Silicone artefact	Small	Anterior	Circumferential
14	Left	5.5	7.7	225	a	Yellow	Yes	Multi	Rupture along ID marks and patch	Large	Posterior	Radial
15	Right	5.3	5.6	330	n	Yellow	Yes	Multi	No distinct features	Small	Anterior & posterior	Radial, circumferential
16	Left	6.7	7.2	270	n	Yellow	No	Multi	Rupture along patch	Large	Anterior & posterior	Radial, u shaped
17	Right	4.8	7	385	n	Yellow	Yes	Multi	Rupture along patch Distinct patch failure	Small	Posterior	Small crack
18	Left	4.6	6	290	a	Yellow	Yes	Multi	No distinct features	Large	Anterior & posteri	Radial, circumferential

	Explant	Site	Time in situ (yr)	Time since production (yr)	Volume (cc)	Gel adhesion	Gel colouration	Former markings	Shell layers ^	Features at rupture site	Rupture size	Rupture location	Rupture appearance
												or	
	19*	Right	5	Unknown	290	a	Light yellow	Yes	Single	No distinct features	Large	posterior	Radial
Total	19	19	101.6	99.4		42.11%		84.21%		57.89%			
Total L		6	32.8	37.8		33.33%		83.33%		66.67%			
Total R		13	68.8	61.6		46.15%		84.62%		53.85%			
Mean			5.35	6.21									
Median			3.9	3.3									
Mode			-	7									
Mean L			5.47	6.3									
Median L			2.5	3.3									
Mode L			-	-									
Mean R			5.29	6.16									
Median R			3.8	2.6									
Mode R			5.8	7									

Results were not analysed statistically, however the following were observed:

- Only slight variation was evident in load to failure
- Smooth PIP devices slightly > resistance *cf* textured
- Patch/seam fails at lower load
- All units passed elongation, tensile set, patch/seam strength tests
- N=1/19 PIP devices failed gel cohesion (no value disclosed)
- N=2/18 PIP explants ruptured under impact resistance (no value disclosed)
- N=5/25 PIP explants ruptured ≤ 2150 (mean 5493, range 300 – 9500) N (no individual values disclosed) under static resistance
- Shell thickness (ø) = 0.66 – 0.95 (average absolute minimum ø 0.45 – 0.66; maximum ø 1.16; lowest 0.35) mm (no individual values disclosed, only distribution plot at Figure 5)

The authors opined that variation in thickness was a common observation but no evidence was provided to scrutinise the contention. They also reported discolouration in all intact and ruptured explants, varying in shade of yellowing, however, molecular weight (mw) analysis of n=1 each of yellow and clear samples of silicone gel did not reveal significant difference in MW distribution of extractable components (no data disclosed).

N=4 (47%) exhibited ruptures involving the patch.

The authors also opined a common feature of parallel marks or grooves on the inner shell surface in 84% of explanted units, which they attributed to machining marks imparted by formers used to shape the shell of the device during manufacture. Other imperfections observed on units were postulated by the authors as potential preferential rupture initiation sites, along with sharp corners and porosities evident in cavities of textured surface. Actual observations, including estimated density and severity were not disclosed.

Analysis of tissue samples apparently revealed significant pathological findings (*nota bene*: not pathologically significant findings) but no actual results were disclosed. Silicone levels ranging from 996 – 4250 mgl^{-1} were assayed in n=5 patients, while tissue samples excided from near intact contralateral side of implant sites yielded 172 – 216 mgl^{-1}.

The authors also considered that while average thickness (ø) of all units tested was 0.57 – 0.95mm, certain regions in nearly all shells exhibited absolute minimum ø <0.57mm, non-compliant with PIP specification. They found lowest ø in valleys of textured surface, as low as 0.35mm. They considered that inferior manufacture process control accounts for the variation in shell ø, particularly as shells were made by hand dipping formers into silicone mix. Other possible factors of shell failure in devices of this kind identified included patch inferiority, consistent with observations by other workers [Brandon *et al* (2003), Mayes and Niessen (2010)] who were cited by Swarts *et al*.

The authors reported that 47% of the ruptures examined involved the patch, 21% involved identification marks and more than half were located on both anterior and posterior surfaces. They observed that the majority of ruptures followed a radial path and that typically, failures on the anterior surface manifested as small, circular cracks.

Biopsy samples taken from the capsule or fibrous tissue revealed synovial metaplasia and marked xanthogranulatomatous inflammation[1]. n=2 cases revealed xanthogranulatomatous inflammation n=1 of which was scored as florid xanthogranulatomatous inflammatory reaction including aggregates of small lymphocytes. Importantly, therefore, their findings contradict and contest conclusions by the NHS expert group who found that the gel filler material used in PIP implants did not pose a threat to human health.

Silicon levels in tissue from near the ruptured PIP implants were elevated as expected, with the highest level of 4250 mg/l recorded. Silicon levels on the contra-lateral side were significantly lower, with the highest level of 216 mg/l well within normal silicon levels for breast tissue.

The authors concluded:

- minimal evidence of shell degradation over average residence in subjects examined (5.3 years)
- Certain quality issues may potentially contribute to shell weakness or shell failure:
  - variable shell thickness
  - and the nature of the shell texturing
  - sharp corners and porosities in cavities of the textured surface
  - machining marks
  - identification marks
  - silicone artefacts on the inner shell surface and welded patches
- The extent and nature of these quality issues makes it difficult to predict implant longevity

In order to examine the data further and to understand relevance and important of observations expressed by Swarts *et al*, we analysed their data by:

- modality of rupture
- characteristics of rupture
- Index of time since production and residence time (*in situ*) of implanted units

[1] Synovial metaplasia is not an uncommon finding for silicone implants and has been described for breast implants and other silicone devices.

Unfortunately, the entire at-risk population remains unknown, therefore, inferential statistics cannot be applied to permit prediction or inference about the population from observations and analyses of such samples.

Modality and characteristics of rupture

Rupture of implanted PIP silicone-filled breast implants was characterised by size of rupture, implant location (left or right breast) and rupture appearance. Appearance of rupture observed was classified by 6 denominators:

- Radial
- Radial and tangential
- Tangential
- Small crack
- U shape
- Circumferential

Assuming that rupture appearance denominators are truly distinct, easy distinguishable and consistent, observations by Swarts *et al* were analysed and plotted histographically and pie-charts produced. Results indicate that radial rupture dominates in the entire implanted population, however, dominance mainly originates from incidence of radial rupture in units implanted in the right breast (Figures 1 and 2). It is impossible to determine whether the differences observed are statistically relevant and conjecture what the causes might be.

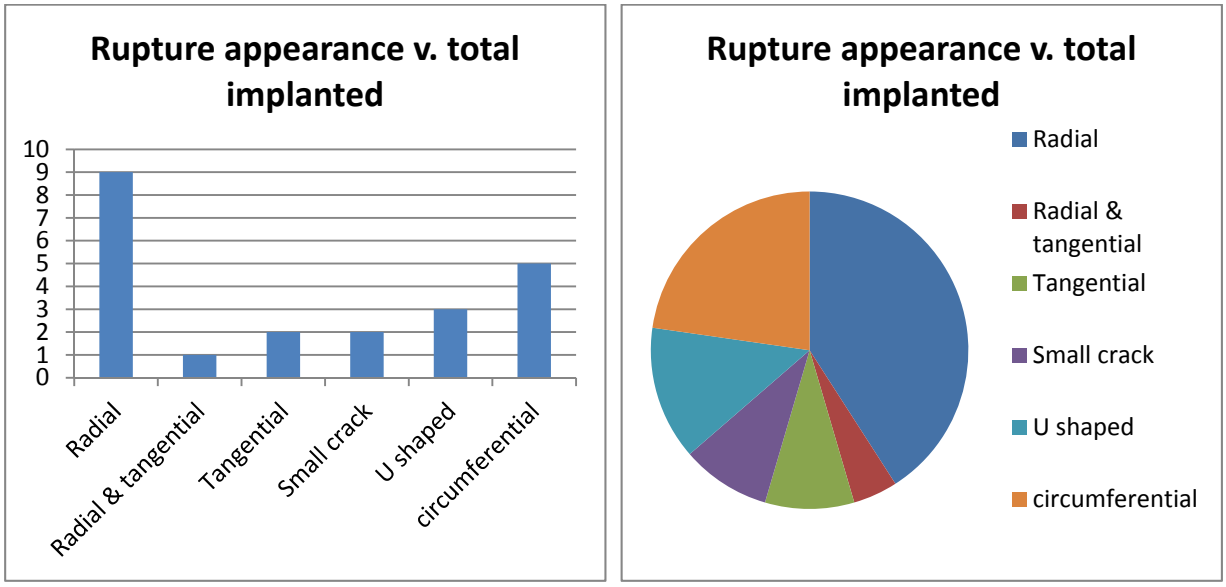


Figure 1 Appearance of rupture in retrieved PIP implants (after Swarts *et al*, 2012)

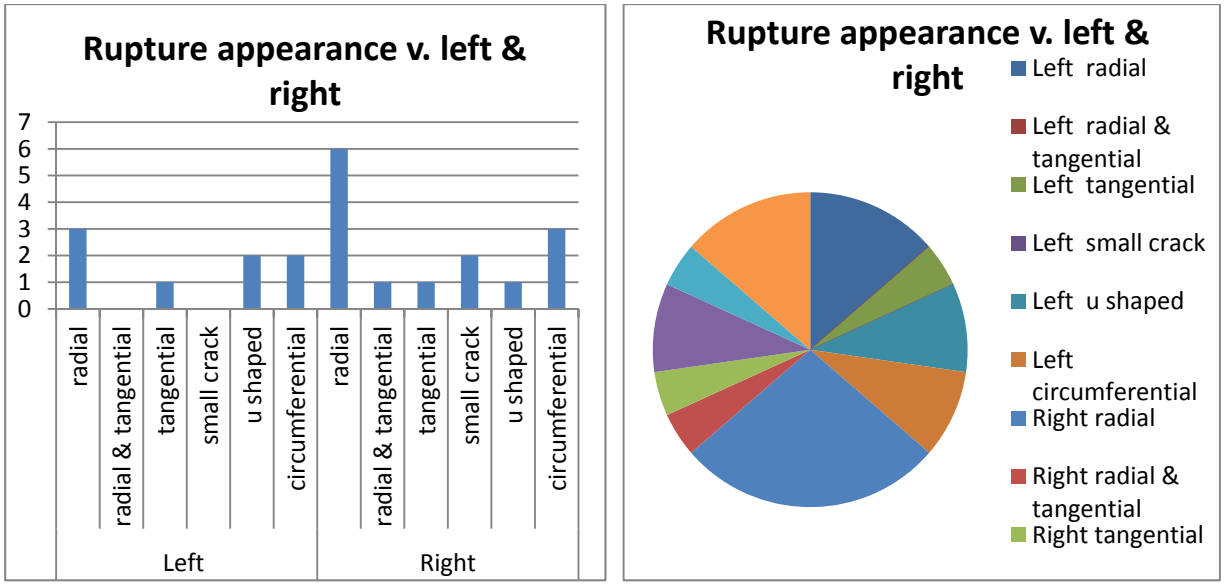


Figure 2 Appearance of rupture in retrieved PIP implants from left and right breasts (after Swarts, *et al*, 2012)

Location of rupture as a function of total implanted reveals coincident anterior and posterior rupture occurs more frequently than anterior or posterior rupture alone (Figure 3). Differences are evident graphically between left and right breast but it is impossible to determine whether differences observed are statistically relevant and conjecture what the causes might be.

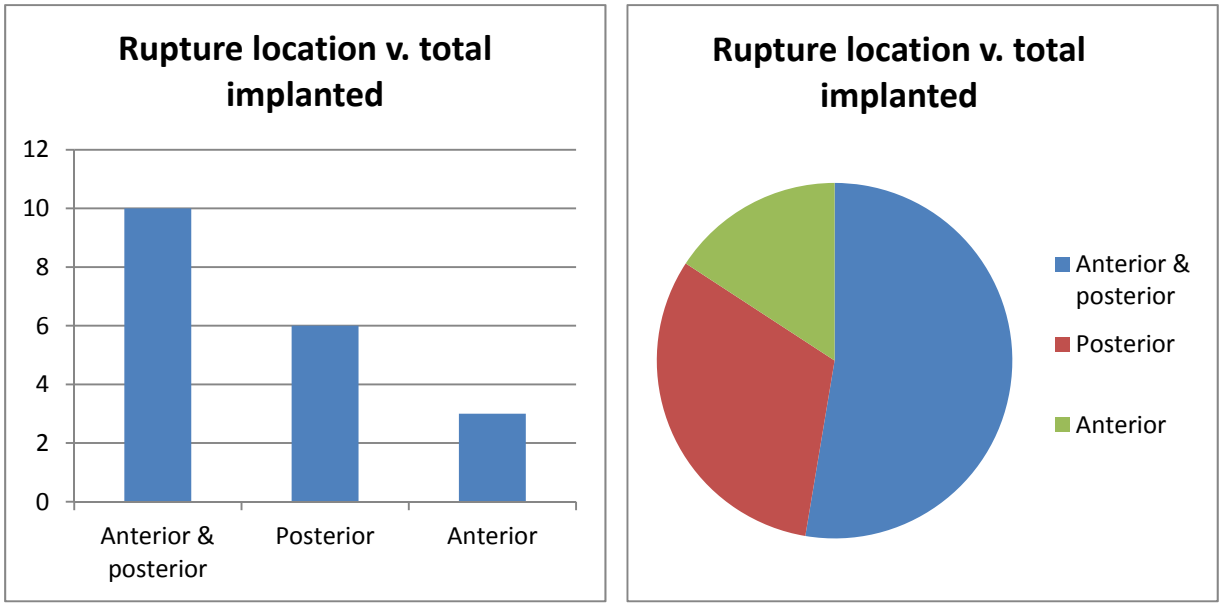


Figure 3 Location of rupture observed in retrieved PIP implants (after Swarts *et al*, 2012)

Relative rupture size (left and right), categorised as small or large does not appear revealing (Figure 4). Considerably further and more critical examinations would be

needed on larger samples of units in order to produce informative observations and permit thorough analysis.

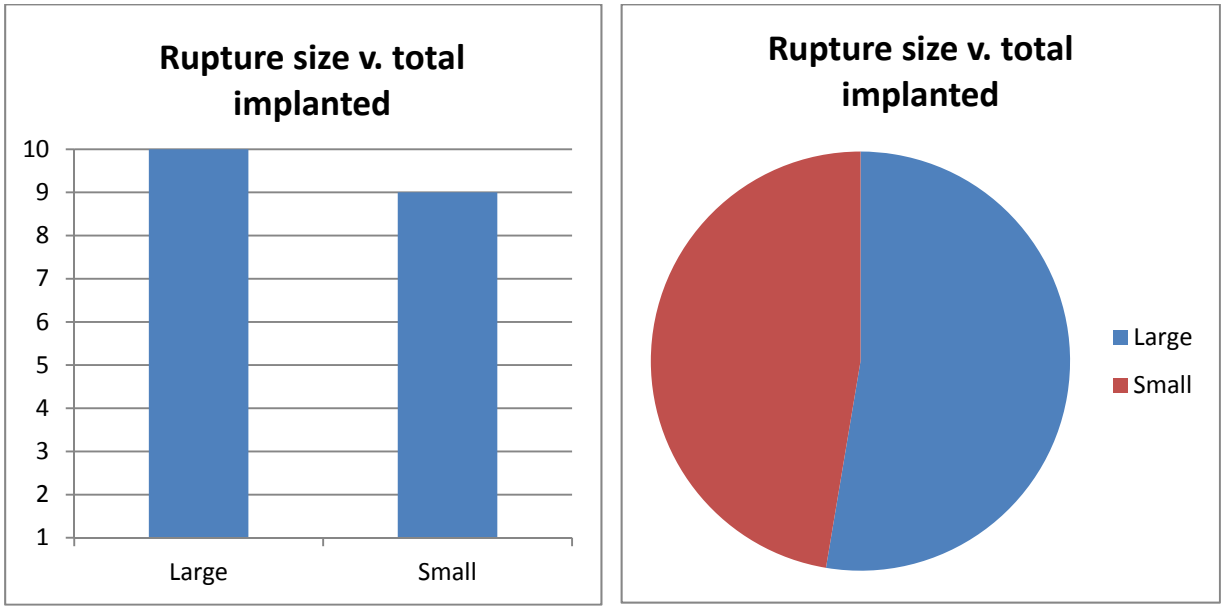


Figure 4 Relative size of rupture observed in retrieved PIP implants (after Swarts *et al*, 2012)

Time to failure

Information in Table 3 was plotted in order to reveal existence of time dependence (Figure 5 Time since production v. time in situ). Total time *in situ* was 101.6 (32.8 left breast implants and 68.8 right breast implants) (mean 5.35) years. There is little evidence suggesting significant difference in longevity between left and right breast implants. Unfortunately, time since production was unknown for implants 8, 10 and 19. Index of average time since production *versus* time *in situ* suggests horizontal linear centrality, however efforts to establish time dependence on data available in the research by Swarts *et al* (2012) proved difficult for several reasons. Since certain information on implants number 7 and 9 was incomplete, they were excluded from calculation of linear average attempting to investigate any relation between durability of implants in the series. Figure 6 indicates a central tendency about respective medians around 6 years since production and 5 years *in situ* time (but interpretation is far from conclusive).

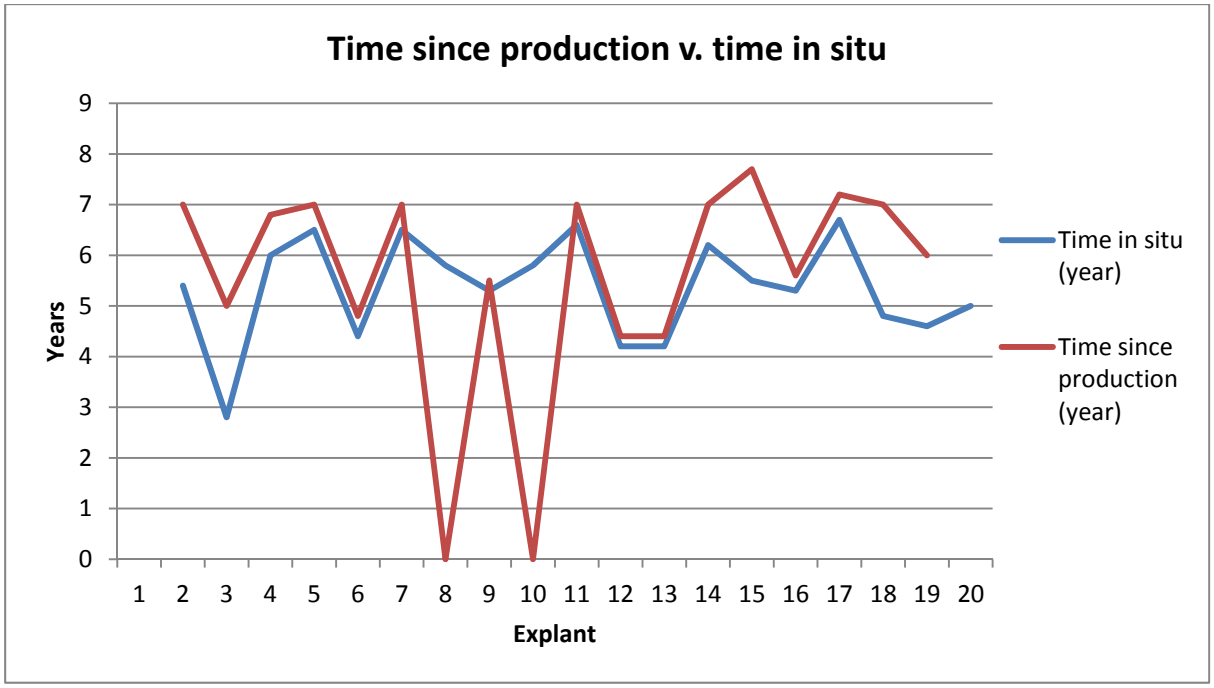


Figure 5 Examination of time to failure from data from Swarts *et al* (2012) on retrieved

Features at the site of rupture were evident in 57.89% of implants retrieved, manifesting in scratch marks, silicone artefacts, propagation along the identification marks and patch or were indistinct.

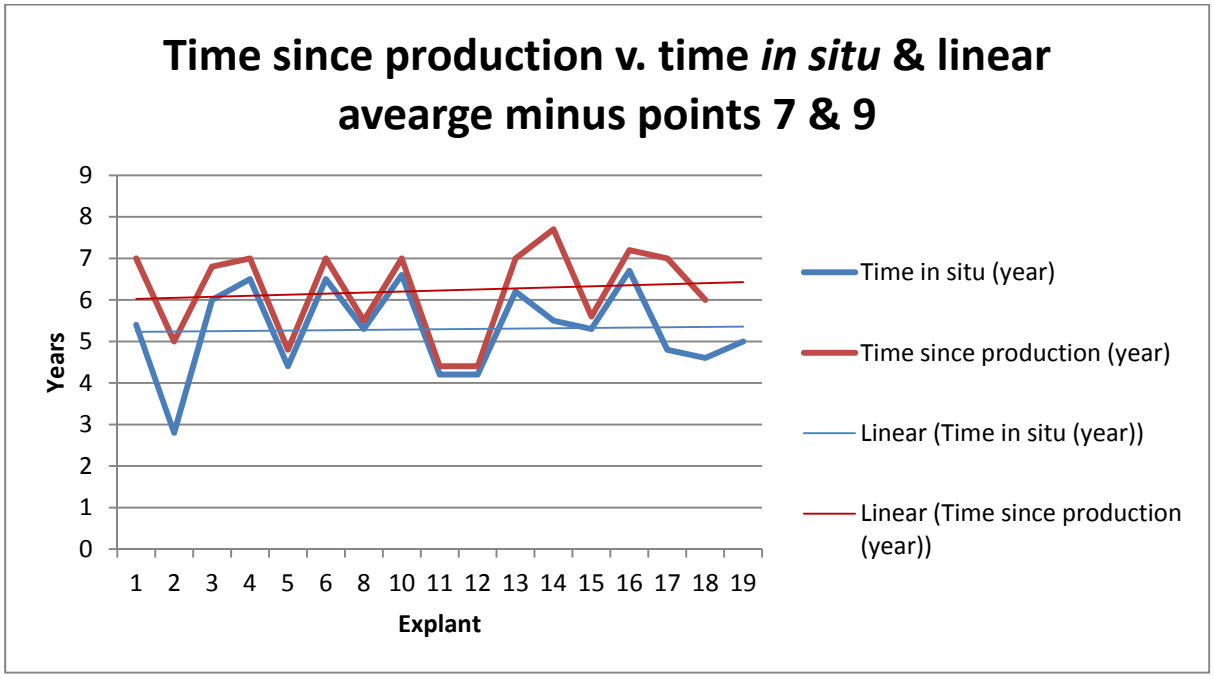
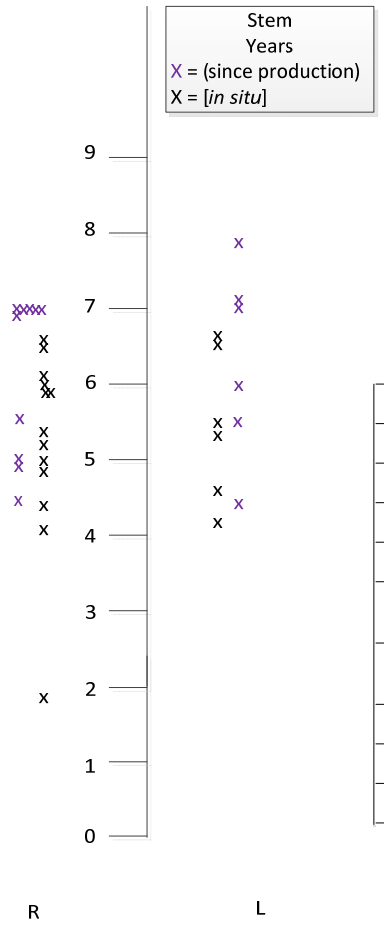


Figure 6 Linear average of time since production *versus* time *in situ*, excluding implant numbers 7 and 9

Distribution of the set of data was examined by a stem and leaf plot (Figure 7). This indicates existence of possible bimodal distribution around 5-6 years (*in situ*) and 5-7 years (*post*-production) but cannot exclude exponential drop in value beyond these times. More data would be needed, particularly as data are absent for various years since production and *in situ*.



R		Years	L	
		1		
2.8		2		
		3		
4.4, 4.2, 4.8	4.8, 4.4	4	4.2, 4.6	4.4
5.4, 5.8,5.8, 5.3, 5	5, 5.6	5	5.3, 5.5	5.5
6.0, 6.5, 6.2, 6.6	6.8	6	6.5, 6.7	6
	7, 7, 7, 7, 7	7		7, 7.7, 7.2
		8		
		9		

Figure 7 Stem and leaf plot

Summary

Critical examination of the retrieval analysis by Swarts *et al* (2012) does not withstand scientific rigour. Although their observations indicated certain properties of explanted units resident in the body for an average *in situ* duration of 5.35 years may be associated with undesirable effects on health of subjects or may indicate durability of the device does not fulfil the State-of-the-Art or other expectations from constructive knowledge, such retrieval studies not only suffer from inadequacy of sample population to permit statistically-relevant analysis but also cannot demonstrate causation unequivocally.

Particularly, the retrieval analysis by Swarts *et al* (2012) does not disclose all data that could permit full scientific scrutiny. Therefore, observations and conclusions therein can only be interpreted with caution and doubt.

Further, wider studies of retrieved breast implants currently marketed commercially would also be necessary in order to understand whether the alleged deficiencies in PIP silicone-filled breast implants is peculiar or symptomatic of general behaviour of such devices in the body.

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Disclosures

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