Same surface, different risk

Evidence based medicine clearly shows
focusing on roughness is not the right approach
to understanding BIA-ALCL

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BIA-ALCL

What we (don’t) know:

Very rare disease

No systematic data collection

Association with breast implants
(de Boer et al., 2018)

No known causation mechanism

Initial driving hypotheses on the cause of BIA-ALCL: bacterial contamination

Rougher surfaces are larger, with a higher the risk of BIA-ALCL

(Loch-Wilkinson et al., 2017 PRS 140(4))

Justification:

- Most BIA-ALCL cases are with textured implants,
  - fewer cases with finer textured implants,
  - no cases (at the time) with smooth implants

Postulate:

- **Same surfaces should have the same incidence of BIA-ALCL**

Numbers used to justify the hypothesis

	Siltex	Biocell	Silimed PU
Worldwide cases of BIA-ALCL (FDA 20.08.2020 update)	~7%	~85%	?
Single-implant BIA-ALCL rate in Australia (Loch Wilkinson et al. 2019)	1:36,730	1:3,194	1:2,596

↓

1. Oversimplification
Rough textures must be worse

↓

2. Oversimplification
PU must be a texture

Numbers that prove the hypothesis wrong

	Silimed PU	Microthane
Surface	Same polyurethane foam	
Confined geographical area	Australia	Western Europe
Period of sales	2008-2015* * until Silimed lost its CE-mark and TGA-Approval due to particulate contamination	
Sales	46,728	46,569
Single-implant cases	18	1
Rate in Confined area	1:2,596	1:46,569
Rate worldwide	unknown	~1:100,000

↓

Significant statistical difference
(p-value: 0,0001)

Numbers that prove the hypothesis wrong

	(Bristol Myers Squib) Surgitek PU
Patients in the U.S.A. until 1991 (FDA 1995)	~110,000
BIA-ALCL cases (FDA 20.08.2020 update)	Maximum 2 (6 cases attributed to 5 manufacturers)
Incidence	Maximum ~1:55,000

Hypothesis: ***A tentative deduction about a phenomenon that can be verified***

→ If verified, it is provisionally confirmed

→ **If proven wrong, it must be abandoned or modified**

Publicly available data proves the surface roughness approach to BIA-ALCL is wrong.

However, focus is still on the classification of surfaces by roughness:

Barr et al., 2017; Atlan et al., 2018; Jones et al., 2018; ANSM (IEM Study) 2018, **none of which globally agreed**

EN ISO 14607:2018, merely descriptive, generally accepted

↓

None of these classifications relates in any way
to the risks of BIA-ALCL or to the implants' performance

↓

A meaningful classification of surfaces
must have clinical relevance

Starting over

What we need to do now?

- Consider other (multifactorial) theories
- Use known data with an open mind
- Learn about relevant product differences

What we need to do moving forward?

- Collect more data, in a standardised form and promote registries
- Work on alternative classification
- Continue to inform patients and encourage awareness

Consider other (multifactorial) theories

- Genetic predisposition: cancer incidence rates in Australia are
  - the highest for all cancers
  - and the second highest for non-Hodgkin lymphomas (after Lebanon)*

  *International Agency for Research on Cancer, WHO

- Manufacturing differences among textures:
  - Salt loss (Allergan) as opposed to residue free techniques (POLYtxt, MESMO)
  - Production controls

- Leachables:
  - unconvincing, smooth and textured would have same incidence of BIA-ALCL

Use known data with an open mind

Looking at numbers again:

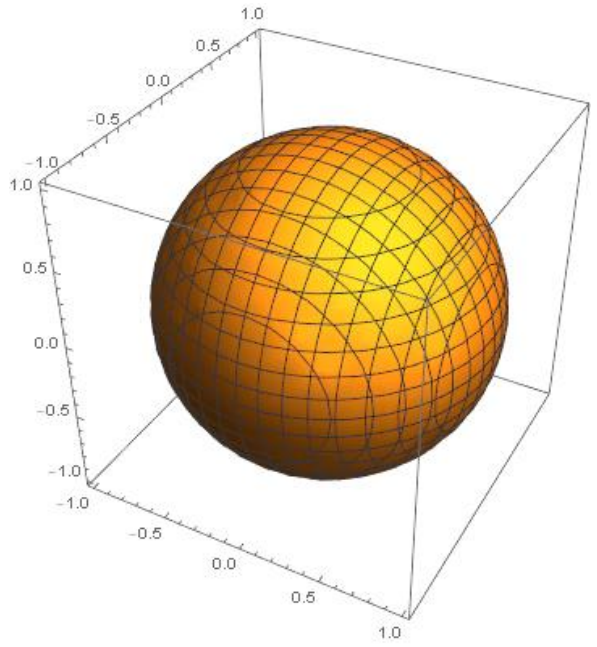
- Allergan Biocell and Silimed PU are ***outliers***

Possible commonalities:

- Particle shedding (Allergan) / particle contamination (Silimed) **(Dutch RIVM study; Webb et al. 2017)**
- Double capsule (Allergan) / delamination (Silimed) leading to seroma **(Hamdi 2019; Hall-Findlay 2011; Spear et al. 2012; Efanov et al. 2017)**

Learn about relevant product differences

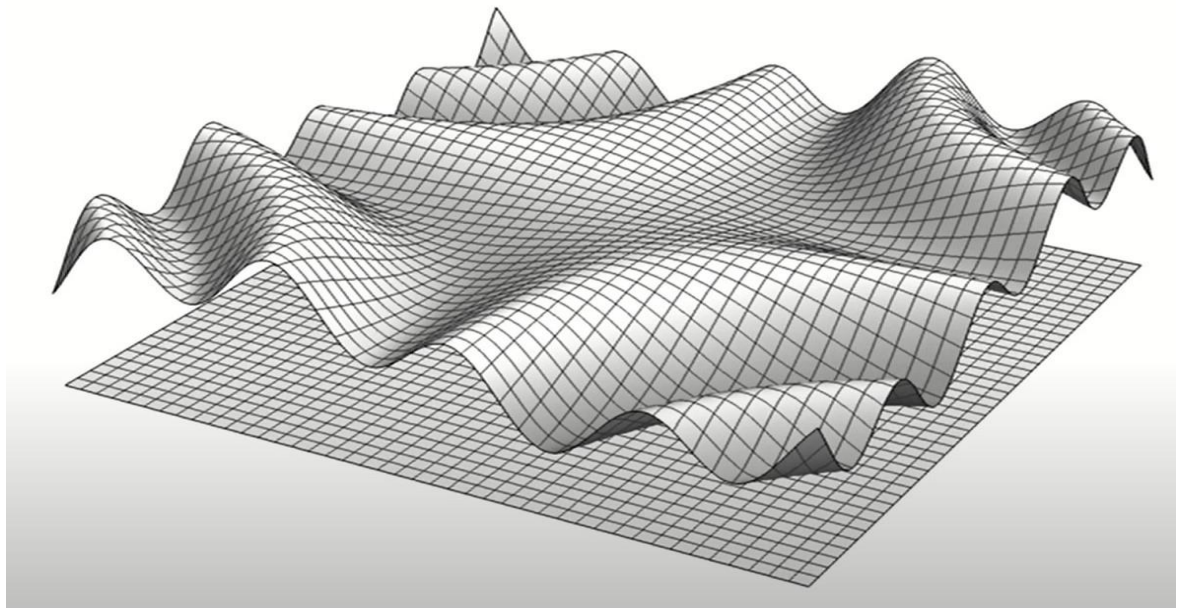
In topology (mathematics) a homeomorphism is the characteristic of two spaces whose surfaces are one the inverse function of the other, and thus correspond.

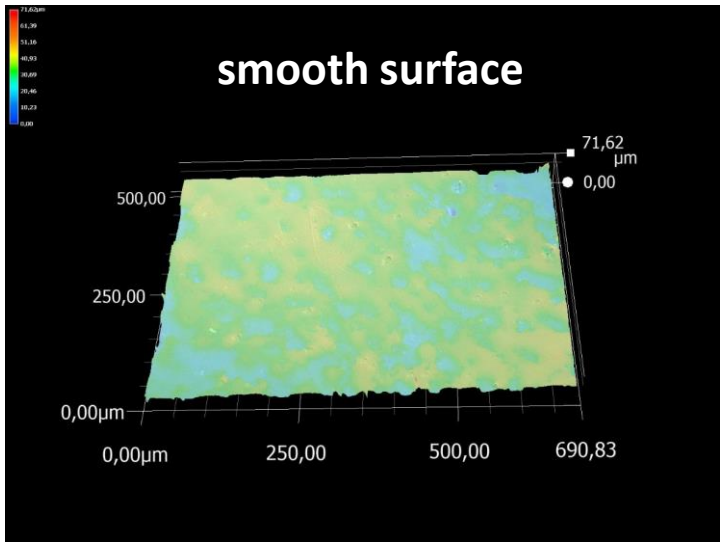


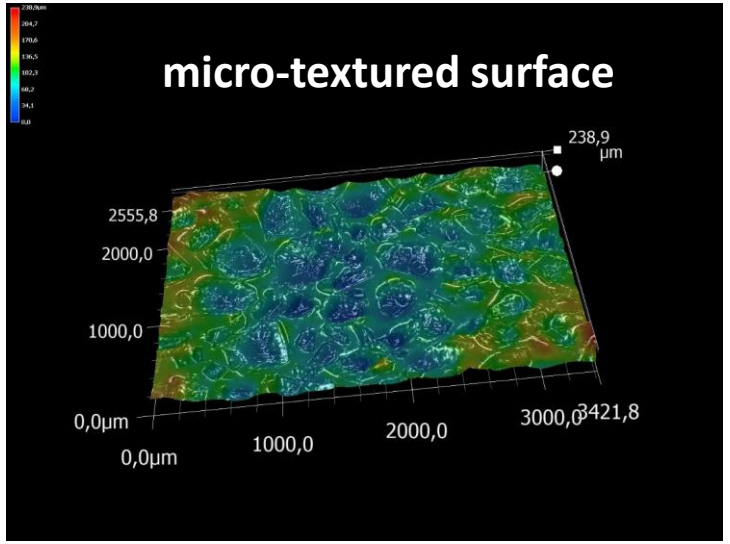
Sphere ←→ Cube
Torus ←→ Cup
Spere ←X→ Torus

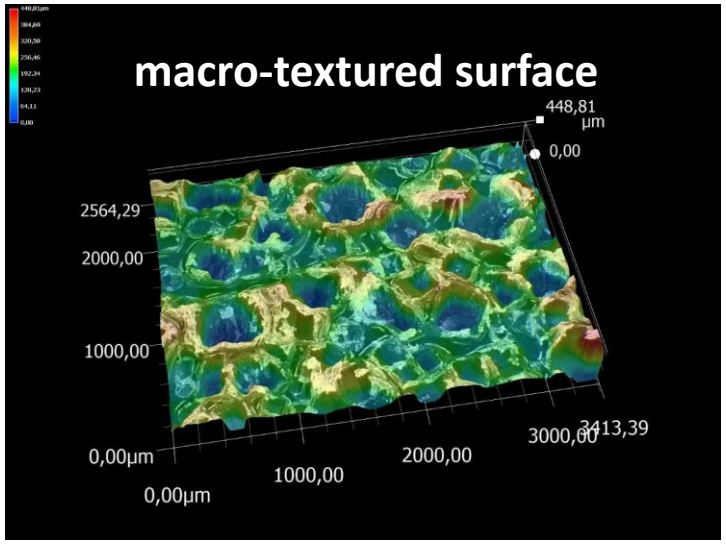
Texture

- Roughened silicone surface
- Created by plastically deforming the outermost non-vulcanised silicone layer of the shell, by several alternative techniques
- Bi-dimensional
- Smooth and textured surfaces are mutually homeomorphic









What does EN ISO 14607:2018, Annex H, say?

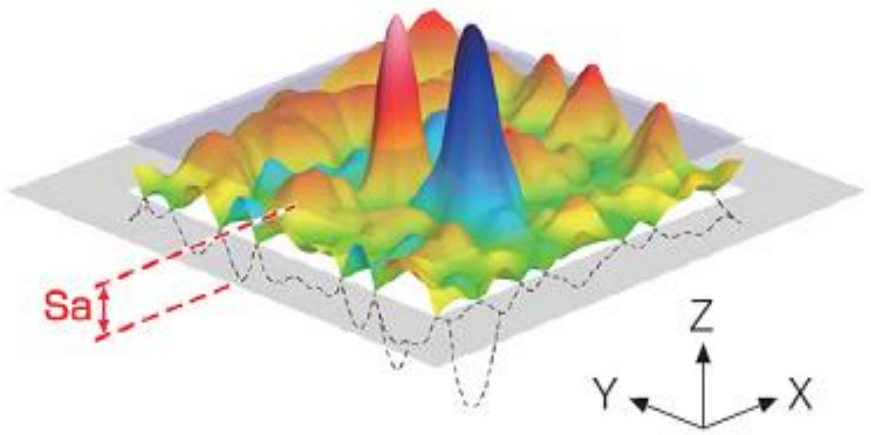
Reference to the average roughness (Sa) of surface, calculated as shown in picture

List of features typical of a solid surface.

While peaks and valleys project into a three-dimensional space, the surface itself is still two-dimensional.

In addition, sample material is the elastomer shell, with no mention of polyurethane

$$Sa = \frac{1}{A} \iint_A |Z(x,y)| \, dxdy$$



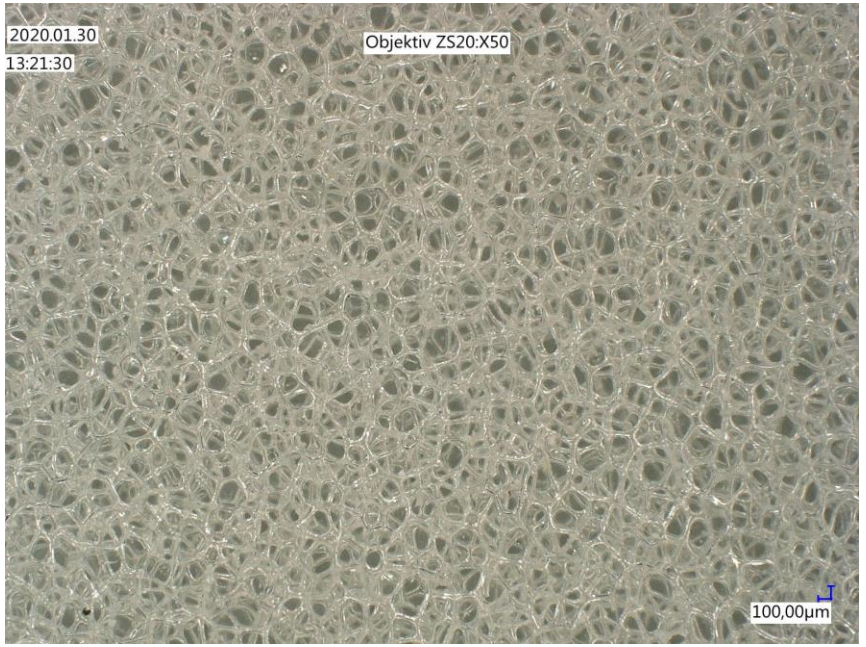
Polyurethane foam

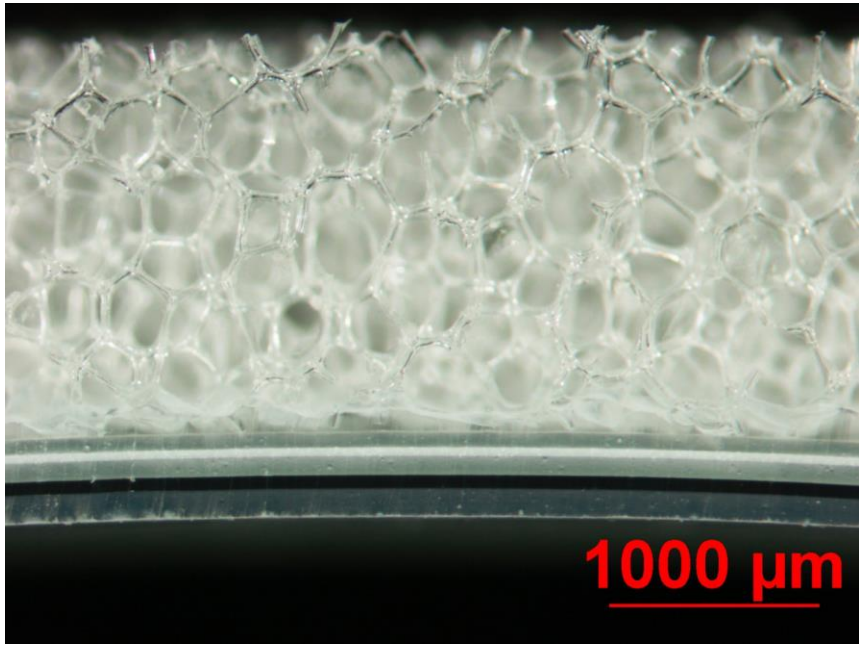
Three-dimensional matrix

Not homeomorphic with silicone surfaces

Different

- Mechanically: not a rough surface
- Functionally: tissue grows ***into*** and not ***onto*** the surface
- Biologically: richly vascularised capsule with active immune cells





Collect more data, in a standardised form and promote registries

Data

- Uniformity and standardization within and among countries
- Collection of complete data sets:
    - type of diagnosis,
    - therapy and prognosis
    - current and prior implant/(s) and respective time *in situ*
    - implantation and replacement/explantation surgeries
    - recent and prior anamnesis
    - history/familiarity with other diseases and respective therapies
- Try to fill existing gaps in previously reported cases

Make breast implants registries compulsory, not only for BIA-ALCL

Work on alternative classification

Creation of standardized registries to collect ***performance*** data of different implant types, surfaces and brands

Possible criteria for classification:

- By rate of capsular contracture, most common complication in breast implant surgery
- By cumulative complications
- By reoperation rate

Continue to inform patients and spread awareness

Joint efforts of physicians, medical associations, manufacturers, distributors, authorities to:

- Provide information
    - to prospective patients
    - to patients who already received implants
- Promote participation in implant registries
- Promote regular controls, with or without symptoms
- Involve other physicians (e.g. ObGyns/Gyns, Family doctors)

Thank you

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