TissueSAFE **plus**

Biospecimen vacuum system

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Problem: formalin in surgery suites.

The International Agency for Research on Cancer (IARC[1]) has classified formaldehyde as a class 1 carcinogen. On December 2013 the EU-REACH adopted a decision to reclassify formaldehyde as a Cat. 1B carcinogen and Cat. 2 mutagen under the EU CLP Regulation. The new classification entered into force on 1 April 2015.
As a Cat. 1 carcinogen, formaldehyde use will be regulated by the restrictive Carcinogens Directive in EU workplaces.
This new classification is encouraging health authorities, surgical staff, pathologists and histotechnicians to look for ways to eliminate the substance from work environments.
Critical exposure points for facility personnel are in the operating suites and in the transfer of tissues in formalin to the pathology lab.

Current drawbacks

- Mounting concerns from surgical and pathology staff regarding the health effects of formalin exposure.
- Facilities can incur significant costs and downtime as a result of a formalin spill.
- Use of formalin can inhibit proper molecular testing.
- Inconsistent documentation of fixation start times from surgery and remote sites.

Solution: elimination of formalin with TissueSAFE plus.

- TissueSAFE plus is an innovative vacuum system which solves the problem of eliminating formalin in the operating theatre and allows a controlled formalin-free transfer of biospecimens to the laboratory. Immediately after excision, specimens are transferred to an adjacent room where the TissueSAFE plus[2,3] is installed.
  Tissue is placed into sterilized specimen bags and sealed under vacuum.
- The sealed specimen bag is then placed into a refrigerated transfer box f at 4 °C.
- A dedicated data logger can be activated at the start of the shift and then placed into the transfer box to continuously monitor and document tissue temperature and transfer time from the surgery suite to the histology lab.
- Specimens arrive (as "fresh" to the laboratory), fixation procedures can now start under controlled conditions in the laboratory.

European Patent	US Patent
EP 2 070 410 B1	US 8,110,346B1

Benefits

- No formalin fumes.
- Specimens are held in "as fresh" conditions.
- No spilling.
- Original specimen colors are preserved.
- Drying of tissues is eliminated.
- Autolytic process is slowed down.

[1] *InternationalAgencyforResearchonCancer(2006)Monographsonthe evaluation of Carcinogenic Risk to humans, vol 88. IARC, Lyon, France*

[2] *Tissue transfer to pathology labs: under vacuum is the safe alternative to formalin. G. Bussolati, L. Chiusa, A. Cimino, G. D'Armento. Virchows Arch. (2008) 452:229-231*

[3] *Vacuum-based preservation of surgical specimens: An environmentally-safe step towards a formalin-free hospital*
Di Novi C, Minniti D, Barbaro S, Zampirolo MG, Cimino A, Bussolati G. Sci Total Environ. 2010 Jul 15; 408(16):3092-5.

How to eliminate formalin in surgical suites.

Activation of data logger
At the beginning of the shift activate (1) the data logger to continuously monitor time and temperature. Place data logger (2) in the transfer cart at 2-4 °C. Place bag with specimen in the chamber and close cover (3).

1

Your choice of fixation protocols

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Formalin fixation? ☑ **Yes**
Selected blocks are inserted in cassettes for fixation in formalin under controlled conditions (eg. FixSTATION)

Molecular studies? ☑ **Yes**
Specimen can be fixed in an ethanol based molecular fixative (eg. FineFIX).

Tissue banking? ☑ **Yes**
Selected blocks can be frozen for tissue banking.

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Improved work conditions in grossing area
Upon arrival, bags are opened. Tissue colors are preserved in a life-like state, allowing better visualization. Specimens can be documented through a macro imaging system (MacroPATH pro-x). After grossing, archive tissue can be placed in the same specimen bag with formalin automatically added for storage purposes (SealSAFE).

How to control fixation: start with fresh tissues in your lab!

Vacuum sealing of the specimens
Specimens are placed in single use special vacuum bags and vacuum sealed.
Use the pre-printed note field or sealable document pouch to include patient data.

2

Full documenting of vacuum sealing
A label is printed with name of hospital ID code of the specimen, date, time and all relevant information.
The label is glued to the sealed bag.

3

Collecting specimens in the transfer cart
During the surgery hours, vacuum sealed specimens are collected

4

Formalin-free surgical suites

Controlled fixation of biospecimens

From the surgery suite to the histopathology lab
Three transfer modules are available:
1. Basic - 2. Large volume with UPS power supply - 3. For car transfer

5

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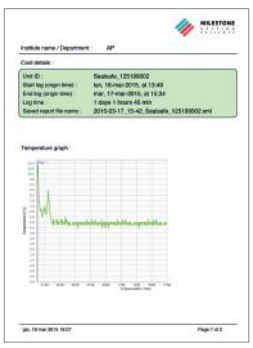
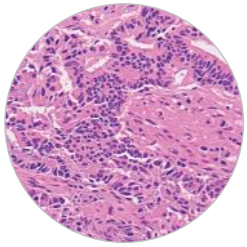
Complete documentation
Download relevant specimen data (time/ temperature), review case reconciliation, and print reports; all from the grossing station.



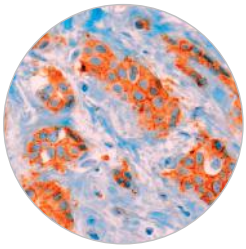
Optimal morphological preservation for up to 72 hours

All tissues specimens.
All tissue types[4] have been preserved under vacuum (colon, gall bladder, spleen, kidney, thyroid, breast etc...) for up to 48-72 hours with optimal histological preservation[5].

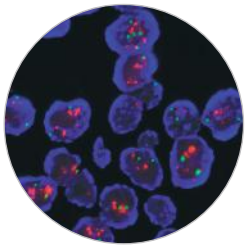
Excellent H&E, HC, IHC, FISH staining properties.
Over a thousand cases, using vacuum preservation, were tracked at the Molinette University Hospital in Turin, Italy. Morphological preservation and immunohistochemical reactivity were excellent and no adverse effects from the process were noted.



H&E
Adenocarcinoma of the colon. The specimen was kept under vacuum at 4°C for 48h, then routinely processed with formalin fixation and paraffin embedding. The structure is preserved and diagnosis is feasible. H&E x 150

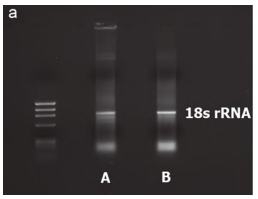


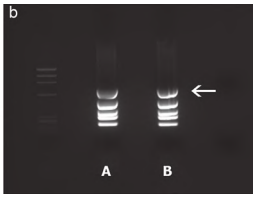
IHC
Infiltrating ductal carcinoma of the breast. The tissue specimen, removed on Friday afternoon, was kept under vacuum at 4°C untill Monday morning (64h), then routinely grossed, fixed and processed. The histological structure is well preserved. Staining for HER2 antigen (Herceptest ™ by DAKO) shows a continuous membrane staining in >30% of cells (3+score).



FISH
Infiltrating ductal carcinoma of the breast. Tissue specimen kept (at the surgical theatre) for 64h under vacuum, at 4°C. Dual-color FISH demonstrates amplification of HER 2 gene (red signal).

Molecular studies. Biobanking.
The quality of RNA preservation is of course related to the time of processing, but even tissues kept under vacuum at 4°C for 48 hours provided nucleic acids of acceptable quality[3].
This finding is in agreement with reports on the stability of RNA in non-fixed surgical specimens kept on ice[4].
Colon mucosa either (A) frozen immediately after removal or (B) preserved under vacuum at 4°C for 48 h. (a) shows 1% denaturing agarose gel of total RNA running: the 18s band is visible and no degradation is appreciable. (b) represents RT-PCR products of cytokeratine 20mRNA of different bp number. The upper band (arrow) is related to a 716-bp product.





[4]Micke P, Ohshima M, Tahmasebpoor S, Ren ZP, Ostman A, Ponten F, Botling J (2006) Biobanking of fresh frozen tissue: RNA is stable in non-fixed surgical specimens. Lab Invest 86:202-211.

[5]Evaluation of tissue preservation using a vacuum-based refrigeration system for specimen transfer from theatre to laboratory D Boyle, R Carson, P Kelly, M Catherwood, S Carroll, L Venkatraman, S McQuaid, H McBride, J James, MB Loughrey, Department of Pathology, Royal Group of Hospitals Trust, Belfast, Northern Ireland.

Images courtesy of Prof. G. Bussolati Turin University (Italy).

Benefits for all

Surgical theatre staff
- No more exposure to toxic formalin fumes.
- No more spilling.

Pathology laboratory staff
- Starting time and length of fixation controlled by the laboratory.
- No toxic fumes. No handling of heavy containers.
- Pre-excised colors are preserved. "Fresh-like" conditions.
- Optimization of antigen retrieval protocols based on laboratory controlled fixation data.
- Possibility for tissue banking.
- Processing with molecular fixatives.

Safety officer
- Compliance with regulatory safety guidelines.
- Reduction of workplace spills and associated costs and downtime.

Hospital administrator
- Elimination of environmental concerns.
- Dramatic reduction in formalin use and lower recycling costs.

The unique features of TissueSAFE plus

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