



Clinical demands for intra-operative imaging in breast cancer

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EPIC Meeting on Photonics for Cancer Diagnostics and Treatment
11-12 December 2019

Ms. de Jong, 42 y old



Referred after breast cancer screening

Symptoms

- -
- No previous breast issues

Hormonal Hx

- Menarche \pm 11 y
- Two children (6y and 4y old)

PM Hx

- No regular medication
- No other medical conditions

S Hx

- Smoker
- 1-2 alcoholic beverages/weekend

F Hx

- Family history of breast cancer (grandmother)

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Diagnostics



Physical examination

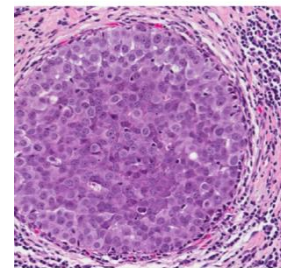
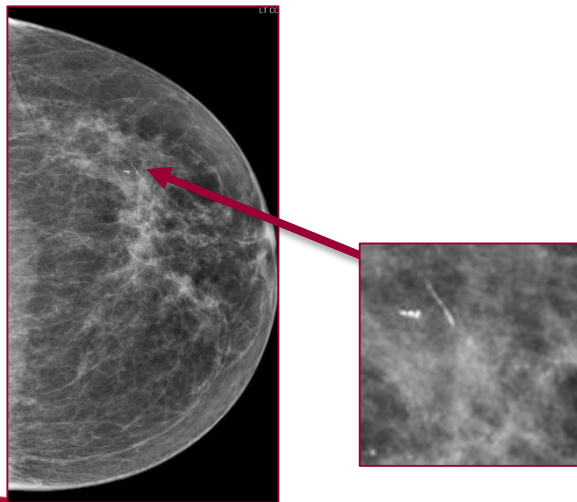


Mammography

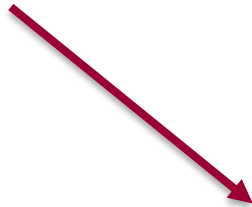


Ultrasound + biopsy

Diagnostics

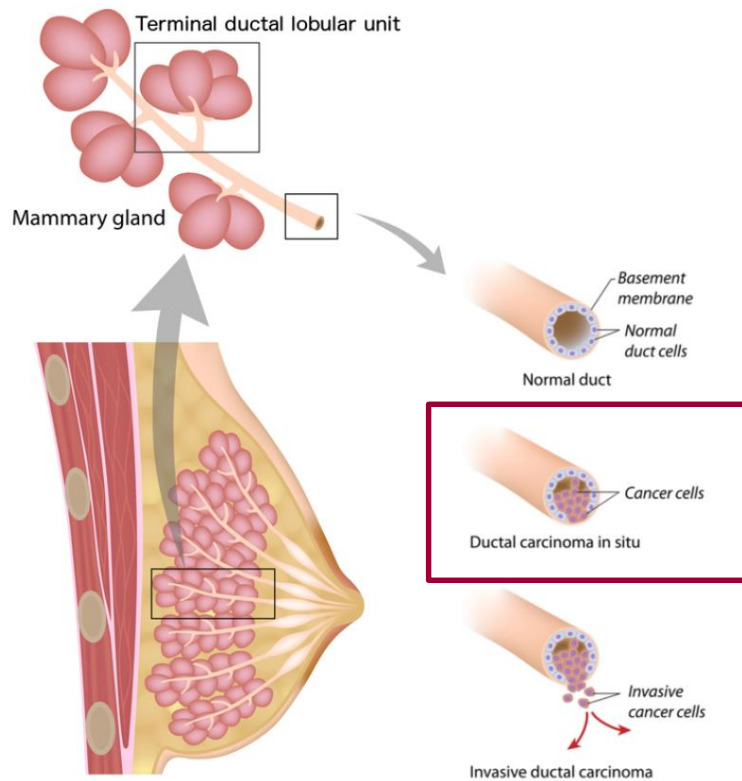


Diagnosis Ms. Young



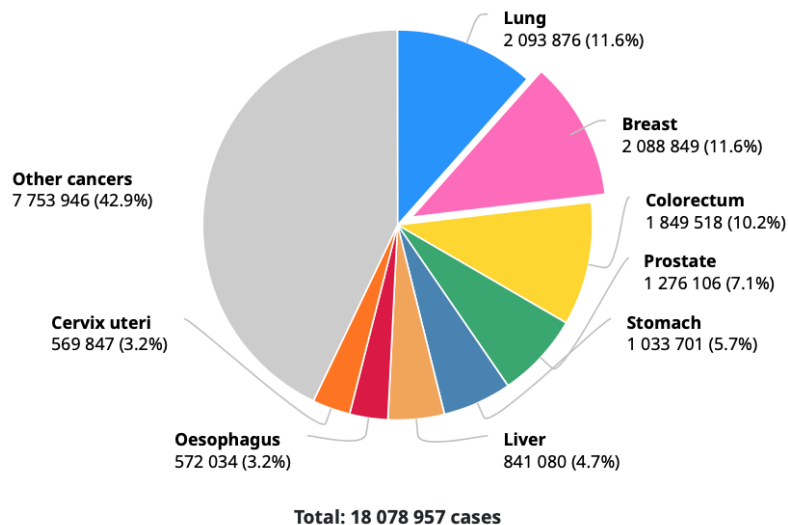
Ductal carcinoma in situ

Breast cancer

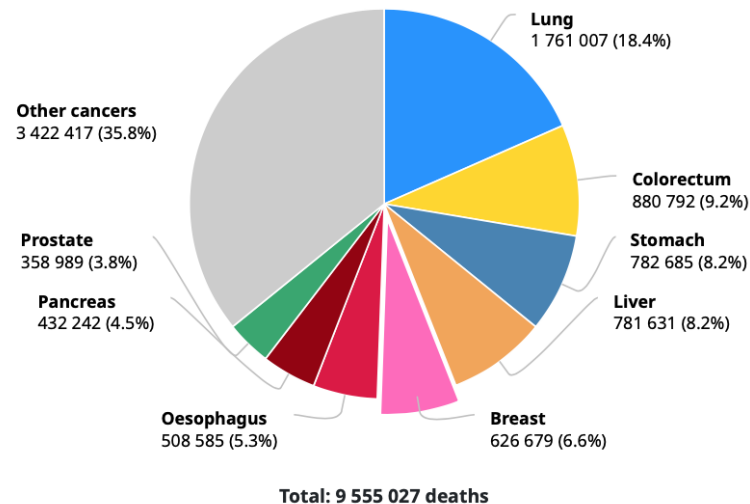


Breast cancer facts (world)

Number of new cases in 2018, both sexes, all ages

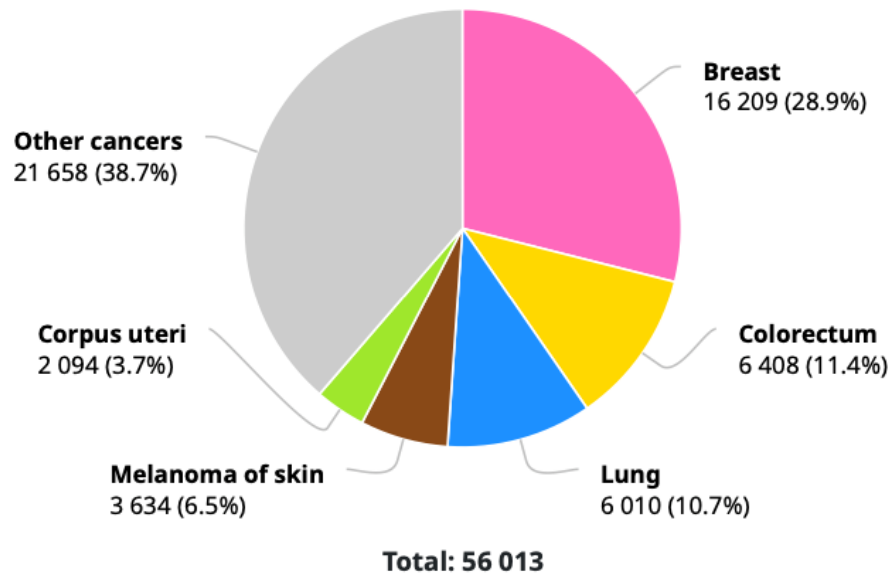


Number of deaths in 2018, both sexes, all ages



Breast cancer facts (The Netherlands)

Number of new cases in 2018, females, all ages



International Agency for Research on Cancer

Treatment options Ms. de Jong



Surgery



Radiation
therapy



Chemotherapy



Hormone
therapy



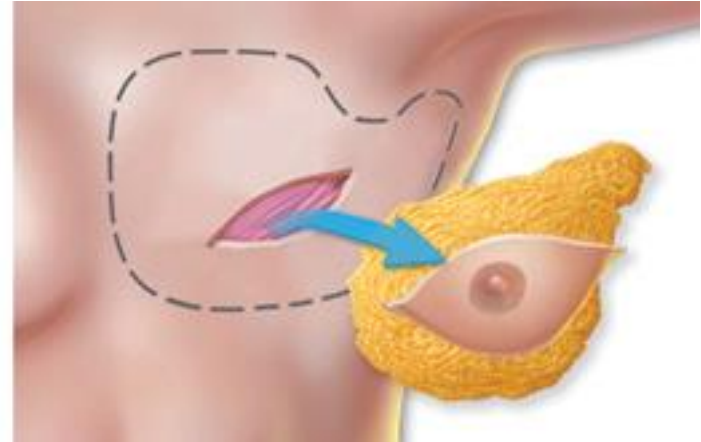
Immunotherapy

Surgery options Ms. de Jong



Breast conserving surgery

60-70%



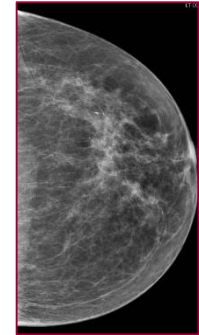
Mastectomy

Surgery

Challenge of removing a non palpable lesion

- Complete tumor removal
- Spare healthy breast tissue

Preoperative imaging



- Location
- Size

Surgery

Challenge

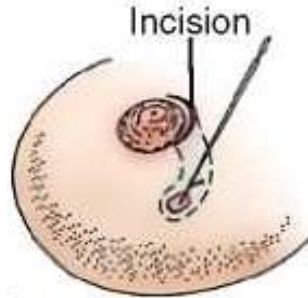
- How to find tumor borders during surgery?
- How to determine if all tumor cells are removed?

Intraoperative tumor localization

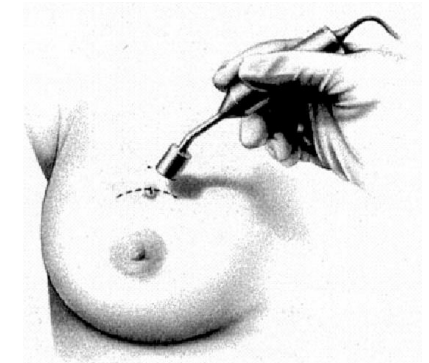
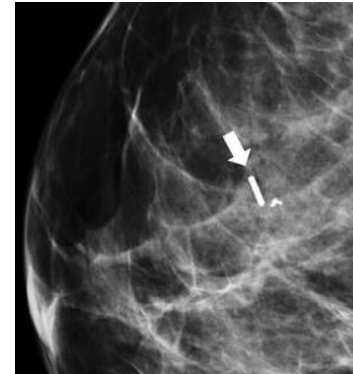
Intraoperative resection margin evaluation

Intraoperative tumor localization during surgery

Wire-guided localization



Radioactive seed localization



- Lack of 3D perspective
- Wire displacement between placement and surgery

- Radiation (legislation required and exposure to patients and health-care workers)

Surgery

Challenge

- How to find tumor borders during surgery?

Intraoperative tumor localization

- How to determine if all tumor cells are removed?

Intraoperative resection margin evaluation

Specimen after surgery

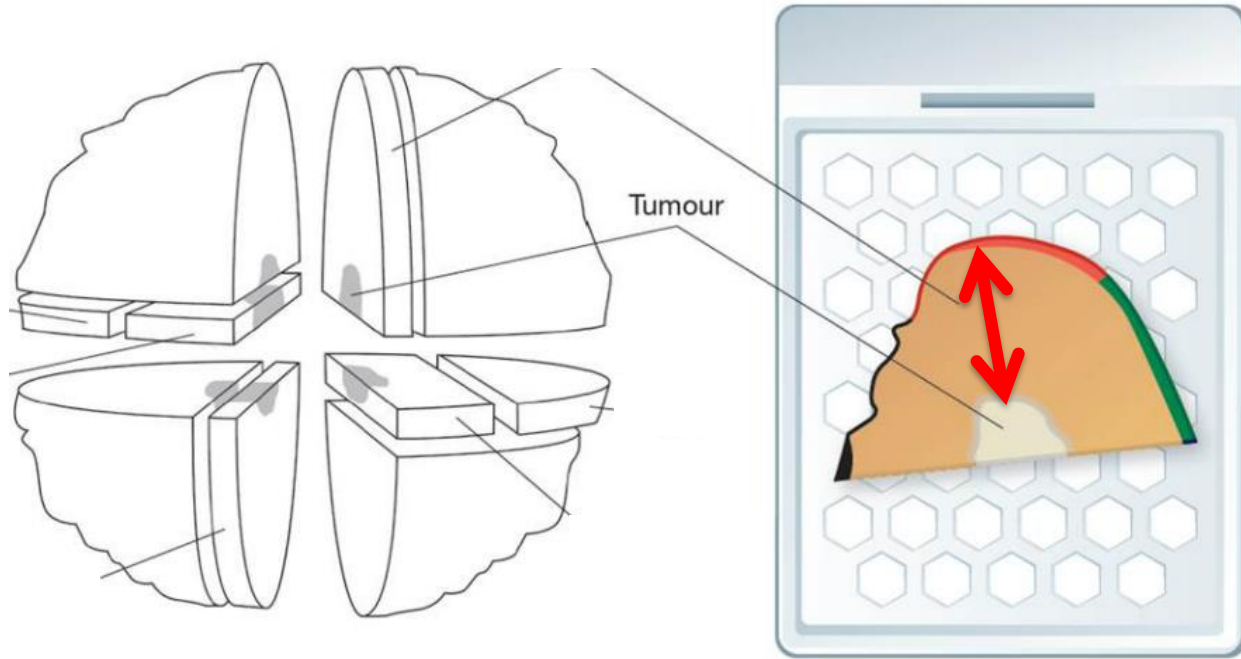


Specimen from the OR

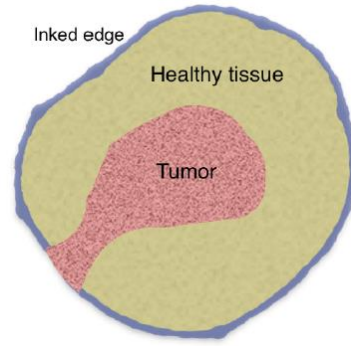


To the histopathology department

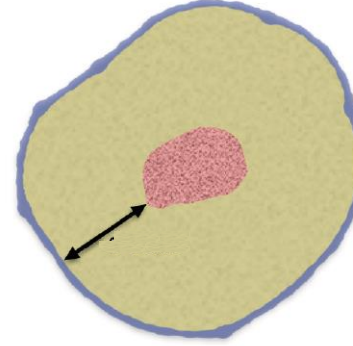
Histopathology



Resection margins



Positive margin



Negative margin



Chance for the tumor to recur

What if...

Accurately localize the tumour

Positive margins could be evaluated during initial surgery directly

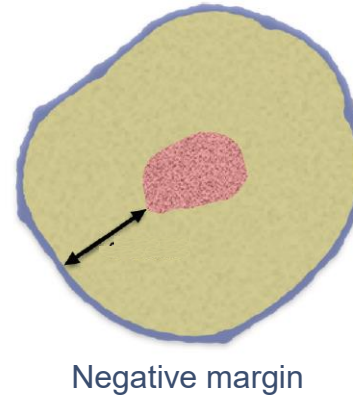
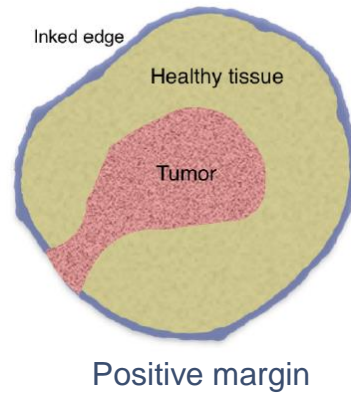
No need to wait for outcome of histopathology

Allows direct intervention

But...

No consensus on definition of positive margin with respect to required sampling depth?

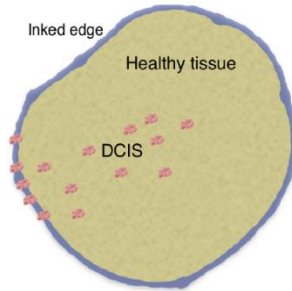
Resection margins



What constitutes an adequate margin of excision?

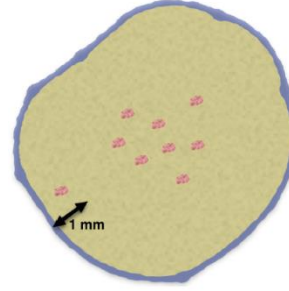
Adequate resection margin: ductal carcinoma in situ

The Netherlands



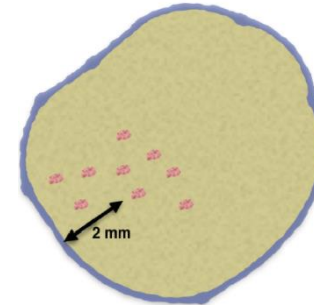
No ink on DCIS

Scotland



No DCIS within 1 mm

Germany
Europe
USA
France
UK



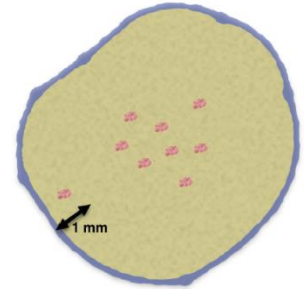
No DCIS within 2 mm

Status of resection margin to express success of surgery?

Year of Publication	Guidelines	IDC	DCIS	Evidence	Country
2009	NICE ³		≥2 mm		UK
	NZGG ⁹	≥2 mm	≥2 mm	10-15	New Zealand
2012	S3-Leitlinie DKG and DGGG ¹⁶	≥1 mm	≥2 mm	8,9,17,18	Germany
	NABON ¹⁹	No ink on tumor over <4 mm surface	No ink on DCIS	20	Netherlands
2013	SIGN ¹⁰	≥1 mm	≥1 mm	17,18	Scotland
2014	SSO-ASTRO ²¹	No ink on tumor ^a		22,23	USA
2015	ESMO ²⁴	No ink on tumor	>2 mm	21	Europe
	St Gallen ²⁵	No ink on tumor		21,22	Austria/Germany
	ABS ²⁶	>1 mm	>1 mm		UK
	Institute National du cancer ²⁷		≥2 mm	28	France
2016	SSO-ASTRO-ASCO ²⁹		≥2 mm	30	USA
	NCCN ³¹	No ink on tumor		21	USA
	JBCS ³²	No ink on tumor		21	Japan

Abbreviations: ABS = Association of Breast Surgery at Royal College of Surgeons of England; DCIS = ductal carcinoma-in-situ; DKG and DGGG = Deutsche Krebsgesellschaft e.V. und Deutsche Gesellschaft für Gynäkologie und Geburtshilfe; ESMO = European Society for Medical Oncology; IDC = invasive ductal carcinoma; JBCS = Japanese Breast Cancer Society; NABON = Nationaal Borstkanker Overleg Nederland; NCCN = National Comprehensive Cancer Network; NICE = National Institute for Health and Care Excellence; NZGG = New Zealand Guidelines Group; PMR = positive margin rate; RR = reoperation rate; SIGN = Scottish Intercollegiate Guidelines Network; SSO-ASTRO = Society of Surgical Oncology–American Society for Radiation Oncology; SSO-ASTRO-ASCO = Society of Surgical Oncology–American Society for Radiation Oncology–American Society of Clinical Oncology.

^aThese guidelines apply to patients with invasive breast cancer treated with whole-breast radiotherapy. It cannot be extrapolated to patients with pure DCIS, to those receiving neoadjuvant chemotherapy or accelerated partial breast irradiation, or to those not receiving radiotherapy.



- Netherlands: **no need** for additional treatment of Ms. de Jong
- UK: **need** for additional treatment

→ Consequences for requirement of a surgical tool:

- Required sampling depth varies between countries?

Surgery

Challenge

- How to find tumor borders during surgery?
- How to determine if all tumor cells are removed?

Intraoperative tumor localization

Intraoperative resection margin evaluation

Requirements smart surgical tool

✓ Acceptable sensitivity and specificity for small lesions and DCIS



Not labour intensive



Acquisition and processing realtime/within minutes



Binary read out



Large sample area and variable sampling depth

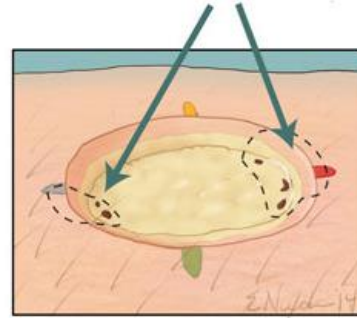
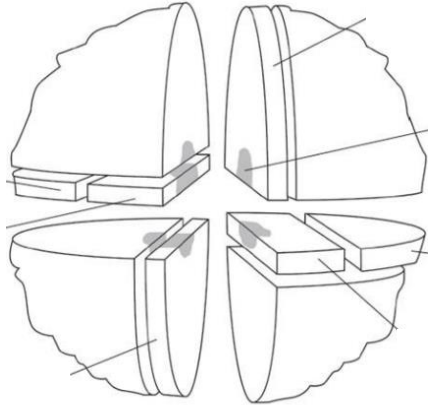


Accessible for all hospitals/not expensive

Can photonics be used to localize the tumor or evaluate whether the tumor is removed completely during breast cancer surgery?

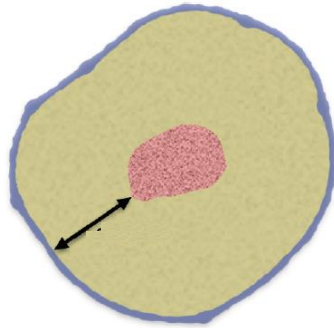
Intraoperative resection margin evaluation

Specimen driven or defect driven



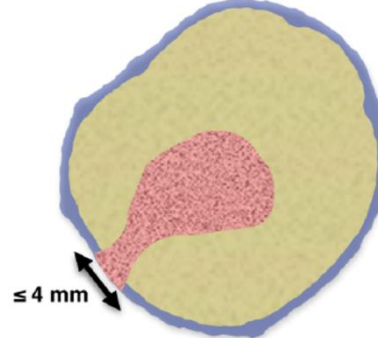
Adequate resection margin: invasive carcinoma

Japan Europe
USA Austria



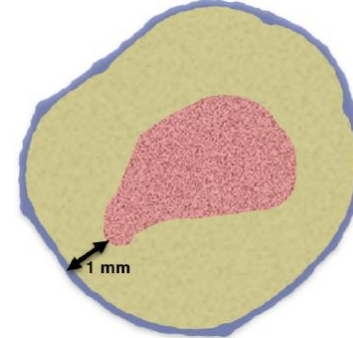
No ink on tumor

The Netherlands



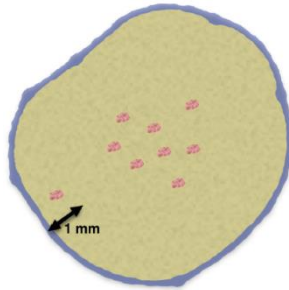
Focally positive

Germany
Scotland UK



No tumor within 1 mm

Outcome surgery Ms. de Jong



Surgery



Radiation
therapy



Chemotherapy

Current techniques available/under development

Macroscopic tumour margin evaluation

Microscopic tumour margin evaluation

Technique	Sensitivity	Specificity
Ultrasound-guided resection	0.25-1	0.74-0.96
Specimen radiography	0.36-0.60	0.60-0.92
Frozen section analysis	0.58-0.92	0.78-1
Imprint Cytology	0.80-0.99	0.85-1
MarginProbe	0.68-1	0.46-0.70
iKnife	1	1
Diffuse reflectance spectroscopy	0.69-1	0.67-1
Raman spectroscopy	0.83-1	0.92-1
Near-Infrared Fluorescence Imaging	-	-
Optical Coherence Tomography	0.55-1	0.68-1

This presentation was presented at EPIC Meeting on Photonics for Cancer Diagnostics and Treatment 2019

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