Het lokaliseren en verwijderen van niet-palpabele mamma-maligniteiten met behulp van een radioactief ^{125}I zaadje

Original article

Localization of non-palpable breast cancer using a radiolabelled titanium seed

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Background: Resection guided by a radiologically placed hookwire is the most common surgical technique for non-palpable breast cancer. This technique has several well described disadvantages such as incidental migration, kinking or fracture of the wire, and difficult logistics between the radiology, surgical and nuclear medicine departments. Use of an iodine-125-radiolabelled (I-125) seed for localization of non-palpable breast tumours could potentially prevent these problems.

Methods: Data on use of the I-125 seed localization technique in 325 consecutive women were collected prospectively between October 2003 and June 2009. All patients with screen-detected, histologically proven malignancy were included. Patients with a preoperative core biopsy showing either ductal carcinoma *in situ* or unclear pathology were excluded from this study.

Results: The mean(s.d.) age of the women was 59·5(11·9) years. Localization was guided ultrasonographically in 275 procedures, stereotactically in 45 and by both techniques in five. The I-125 seed was removed by surgery after a mean of 4(5) days. The mean duration of operation was 62·9(21·2) min. Complete tumour removal was achieved in 310 procedures (95·4 per cent).

Conclusion: Localization of impalpable breast cancer using a I-125 seed was safe and led to a high proportion of radical lumpectomies.

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Introduction

Nationwide breast cancer screening in combination with improved imaging techniques has led to an increased incidence of non-palpable breast lesions[1,2]. In addition, owing to the increased use of preoperative radiologically guided core biopsies, diagnostic surgical interventions have decreased[3–5]. As these impalpable lesions are usually small, they are suitable for breast-conserving therapy.

A complete excision is mandatory in breast-conserving therapy. Therefore, for non-palpable breast cancer, the exact radiological localization of the lesion is an important determinant in achieving a high complete resection rate.

The usual method of localizing non-palpable lesions is by use of a radiologically placed hookwire. This technique has several well described disadvantages such as incidental migration, kinking or fracture of the wire[6,7]. Furthermore, as it is advised that hookwire localization is performed on the same day as the surgical procedure to prevent migration, there may be logistical problems. With this technique, 20–50 per cent of excisions are incomplete[8].

As a result, alternatives to hookwire localization have been developed. Carbon[9] and ultrasound-guided resection[10], as well as the use of radioactive tracers such as technetium-99m[11–13] or iodine-125-labelled (I-125) seeds[14], have been described. In 2003 the technique of I-125 titanium seed localization, as described initially in 2001 by Gray and colleagues[14], was introduced to the breast clinic of Catharina Hospital. With this technique an I-125 titanium seed is placed in the centre of the lesion under mammographic or ultrasonographic guidance. Subsequently, excision of the lesion is guided by a handheld γ probe.

The aim of this study was to evaluate an experience with the I-125 seed localization technique in breast-conserving

Algemene resultaten ^{125}I procedure

2003 - 2009	554	
invasief	**472**	
DCIS	**82**	
	mean	min-max
leeftijd	**58,3**	**32,1 – 82,5**

Algemene resultaten ^{125}I procedure

2003-2009	n=554	Invasief en DCIS
Lokalisatie techniek	stereotactisch	echo
	68	**486**
Dagen in situ	mean	min - max
	4	**1-28**
Aantal zaadjes	1	> 1
	510	**44**

Operatie resultaten ^{125}I procedure

2003-2009	n=472	invasief
	mean	min-max
Operatie duur	**62.9**	**35 – 160**
sn procedures	**Geen problemen**	
Arts-assistent	**95% van de ingreep**	**onder supervisie**

Operatie resultaten ^{125}I procedure

2003-2009	n=472	invasief
	mean	min-max
Tumor afmeting (mm)	**14**	**6-50**
Volume specimen (cm^3)	**113,7**	**10-440**
Gewicht specimen (g)	**40.9**	**6.5-284.1**

Resultaten invasieve tumoren ^{125}I

jaar	Invasief	irradicaal invasief	% irradicaal invasief
2003	60	6	10
2004	73	2	3
2005	70	2	3
2006	68	2	3
2007	72	3	4
2008	56	4	7
2009	73	5	6
totaal	**472 (412*)**	**24 (18*)**	**5 (4*)**

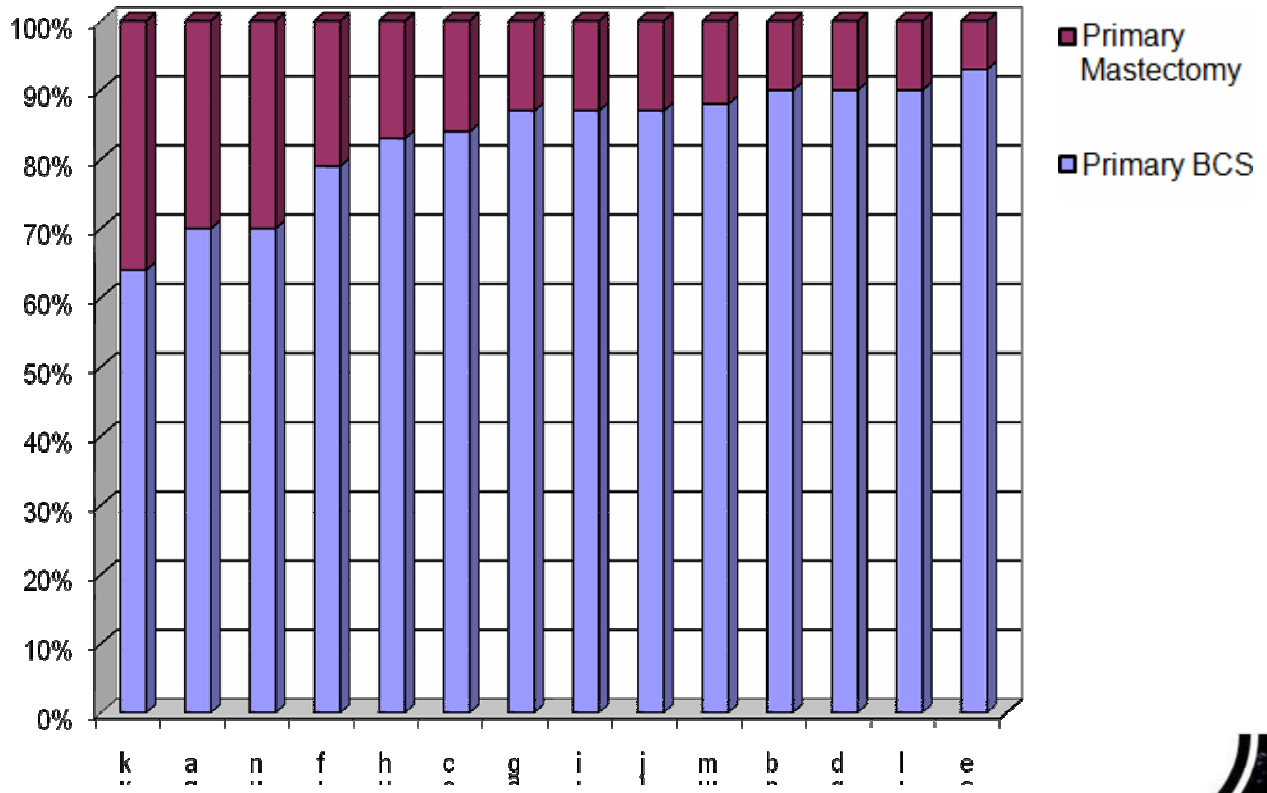
Resultaten DCIS ^{125}I

jaar	DCIS	Irradicaal DCIS	% irradicaal DCIS
2003	6	4	67
2004	14	2	14
2005	13	2	15
2006	10	1	10
2007	11	3	27
2008	11	2	18
2009	17	5	23
totaal	**82 (76*)**	**19 (15*)**	**19 (16*)**

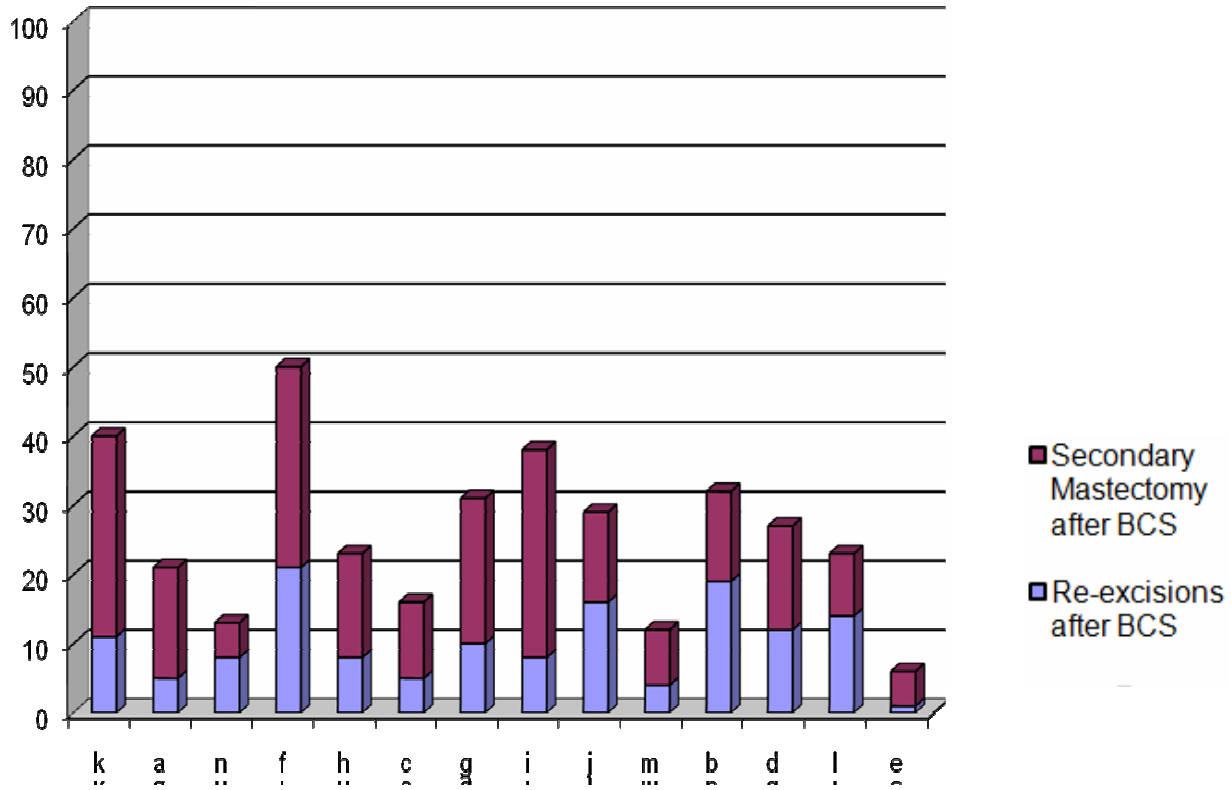
Totaal aantal mammasparende behandeling

jaar	totaal	totaal lumpectomie	totaal irradicale lumpectomie	% totaal irradicale lumpectomie
2006	161	136	8	6
2007	177	148	7	5
2008	190	146	9	6
2009	196	140	10	7
totaal	724	**570**	**34**	**6**

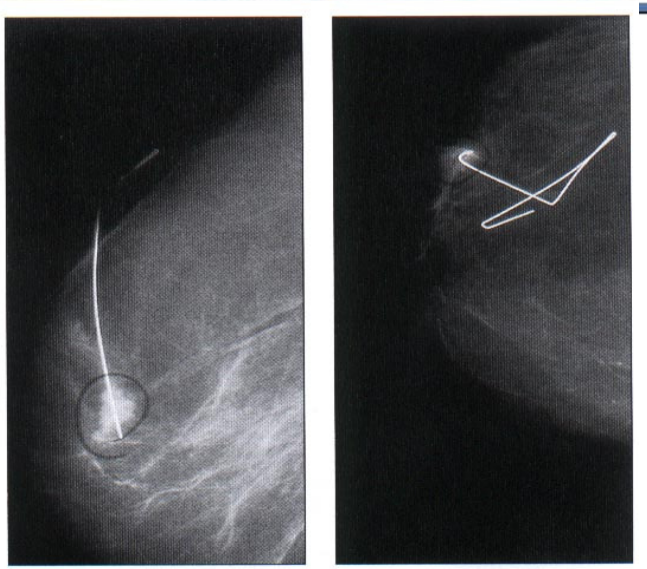
Percentage primary BCS and Mastectomies sorted by hospital in patients with screen detected early stage invasive breast cancer from 1999-2005.

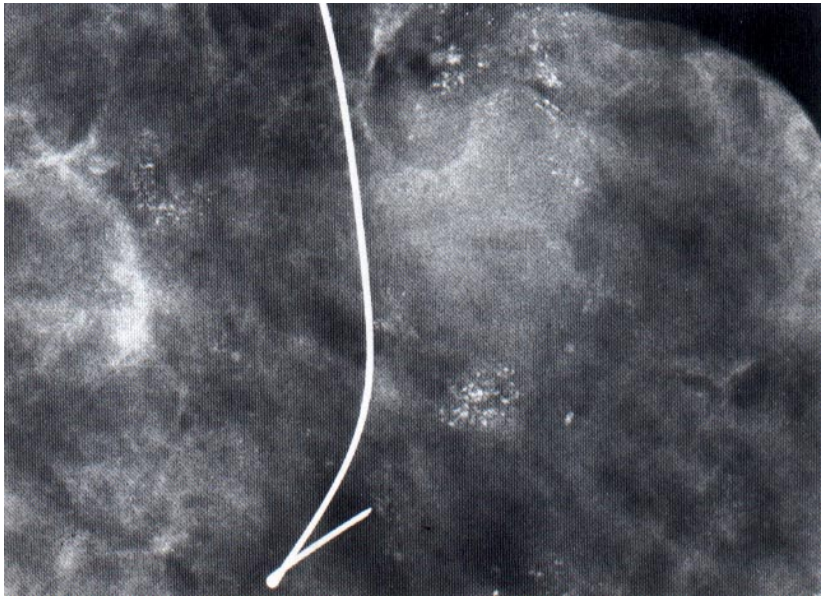


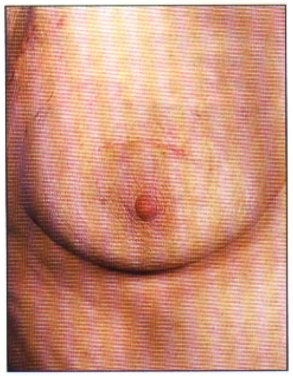
Percentage re-excisions and secondary mastectomies after primary BCS sorted by hospital in patients with screen detected early stage invasive breast cancer.

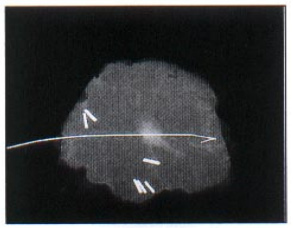


- **situatie voor maart 2003: verwijdering op geleide van het localisatiedraadje**









Gray RJ, Salud C, Nguyen K, et al.

Randomized prospective evaluation of a novel technique for biopsy or lumpectomy of non-palpable breast lesions: radioactive seed versus wire localization.

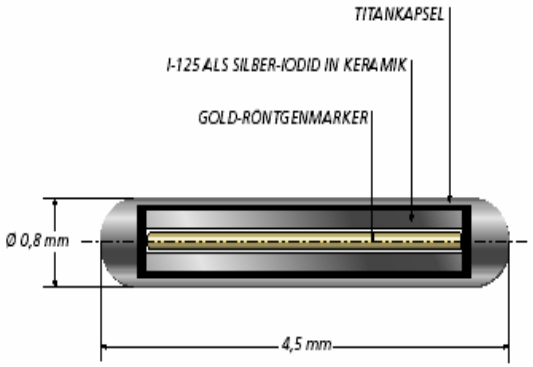
Ann Surg Oncol 2001; 8: 711-715

Het ^{125}I zaadje

- **Titanium (MRI-compatibel)**
- **afmeting: 0,8 bij 4,5 mm**
- **radioactief I-125 in poedervorm**
- **halfwaardetijd 60 dagen**
- **activiteit : 7MBq**

  (diagnostische toepassing)
- **energiepiek: 27 keV,**

  gammastraling
- **gammadetector/probe**



- stralenhygiënische aspecten
- effect op röntgenfilm en MRI
- mogelijkheid van dislocatie
- effect van diathermie en microtoom
- fantoomtesten
- introductiematerialen

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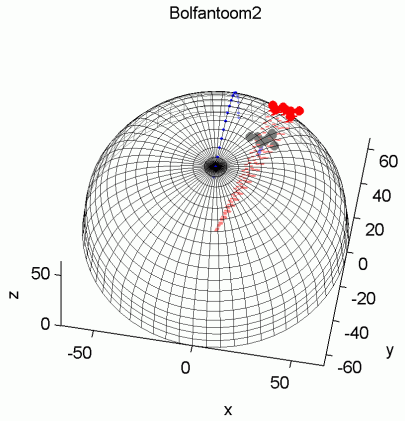
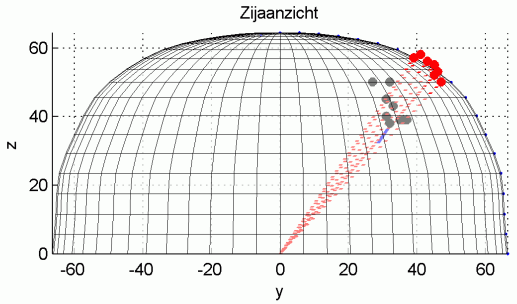
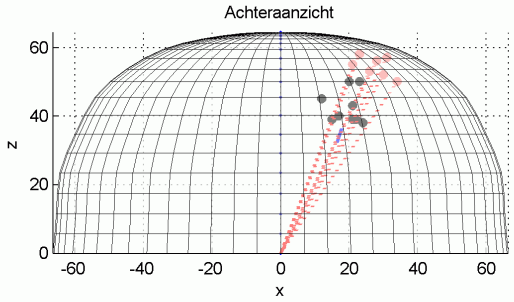
localiseren in vivo

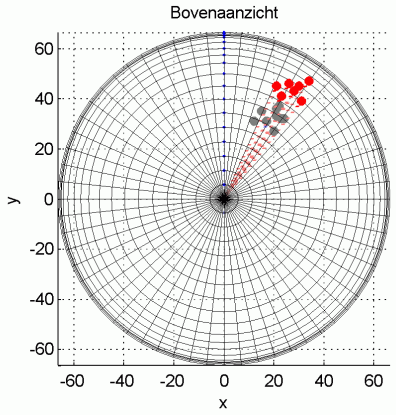
	1e serie	2e serie
Blok	8 ± 4 mm	5 ± 4 mm
Bol x-y	7 ± 3 mm	4 ± 2 mm
Bol x-y-z	10 ± 3 mm	8 ± 4 mm

localiseren in vivo

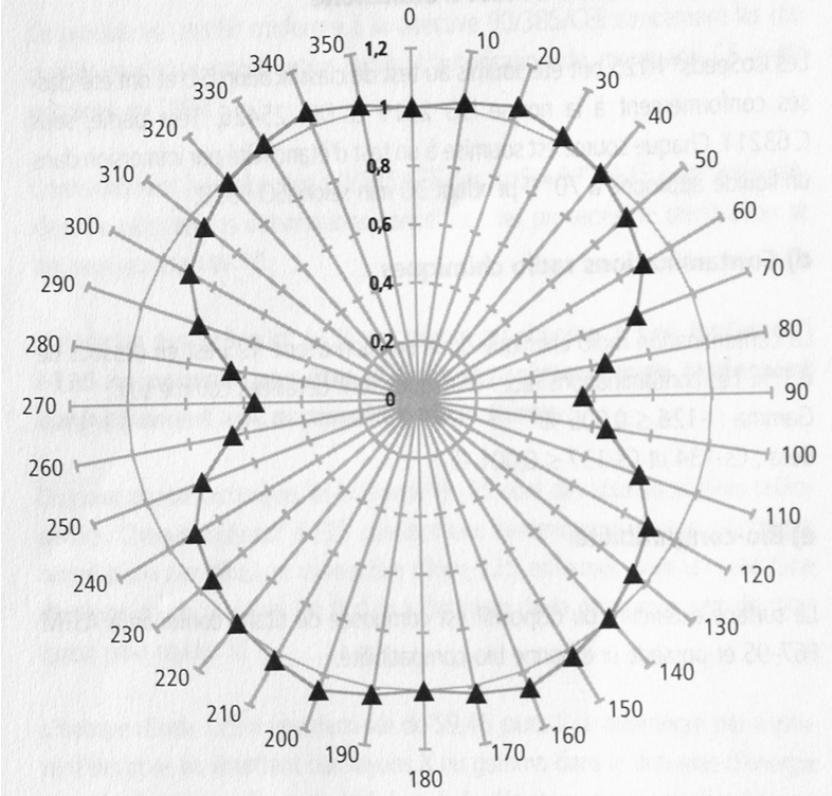






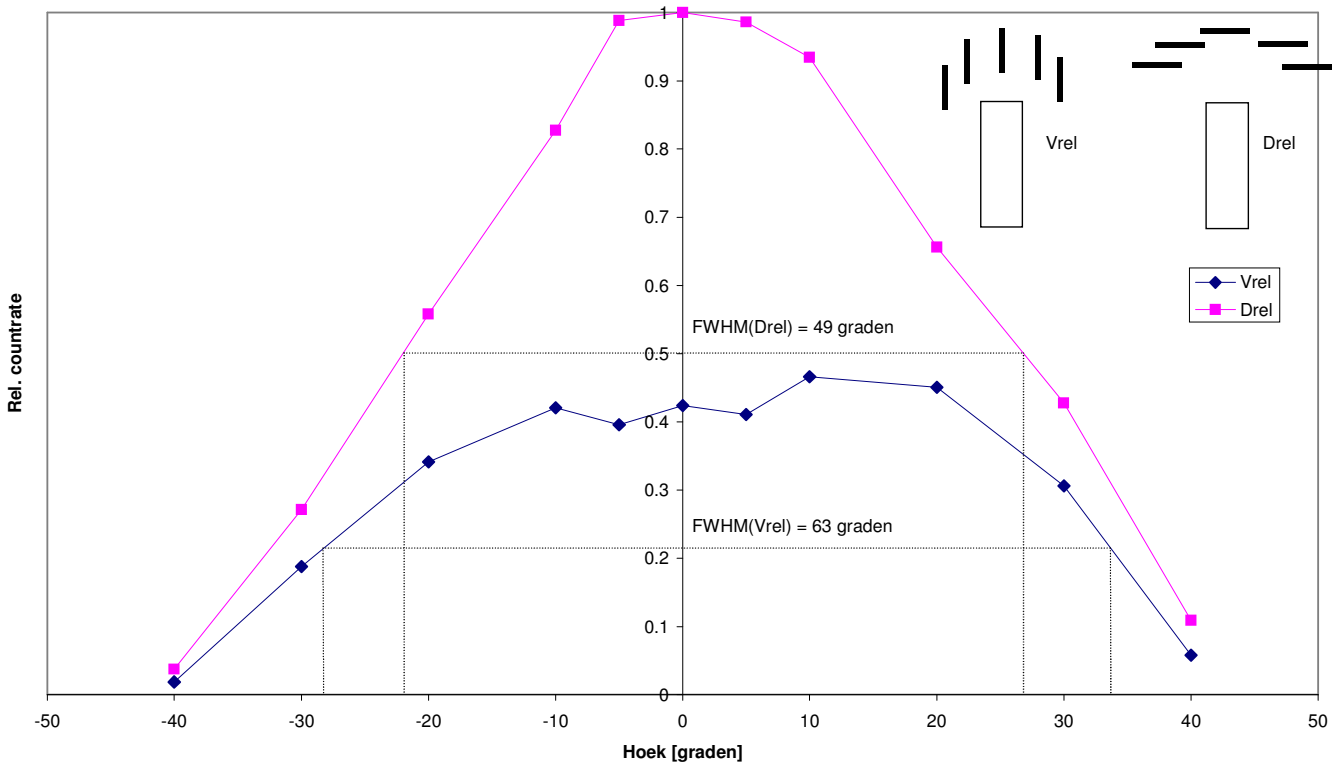


^{125}I localiseren in vivo



Anisotropy of dose distribution at 1cm distance of the centre of the ^{125}I seed (Monte-Carlo count, from the instruction ^{125}I seed of Bebig)

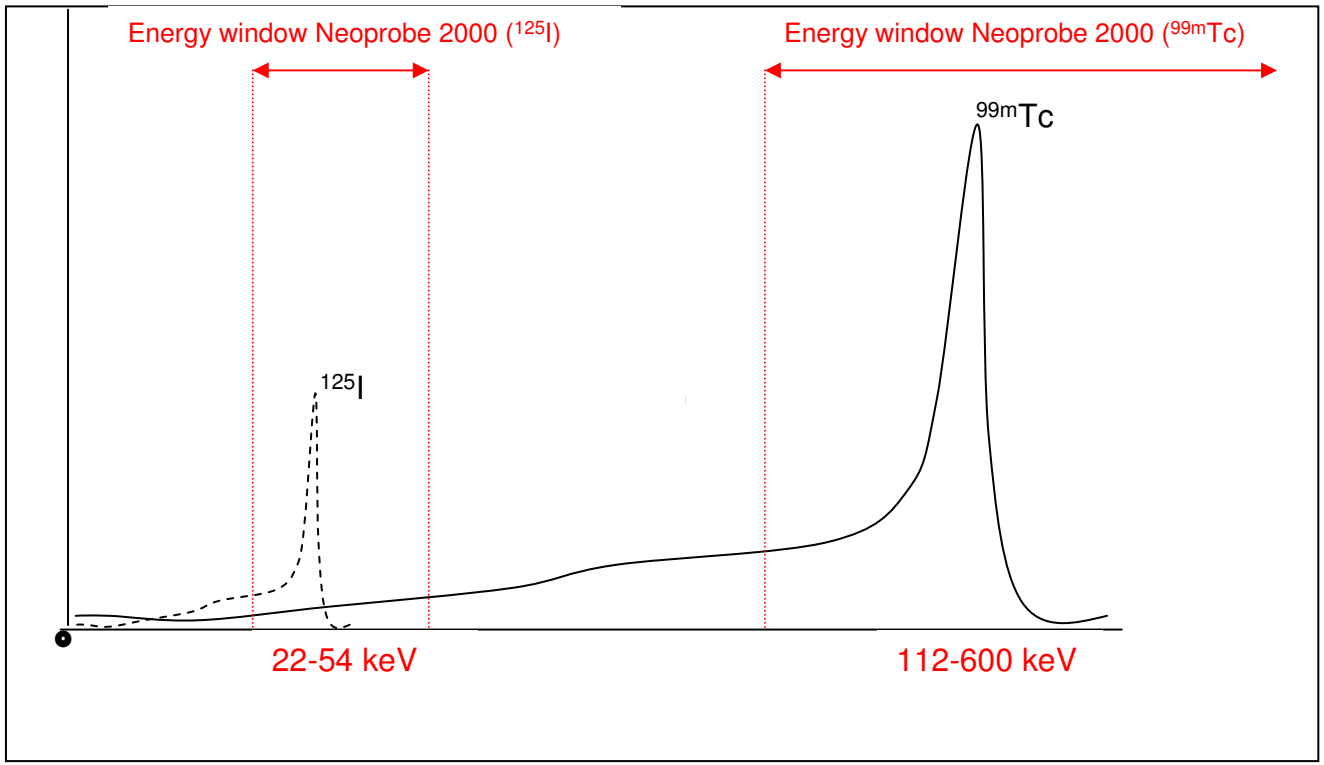
^{125}I localiseren in vivo



The relative countrate measured towards the perpendicular direction (Drel) and the axial direction (Vrel) of the ^{125}I-seed (3.9 MBq) at 5 cm of the Neoprobe 2000 in the air with collimator.

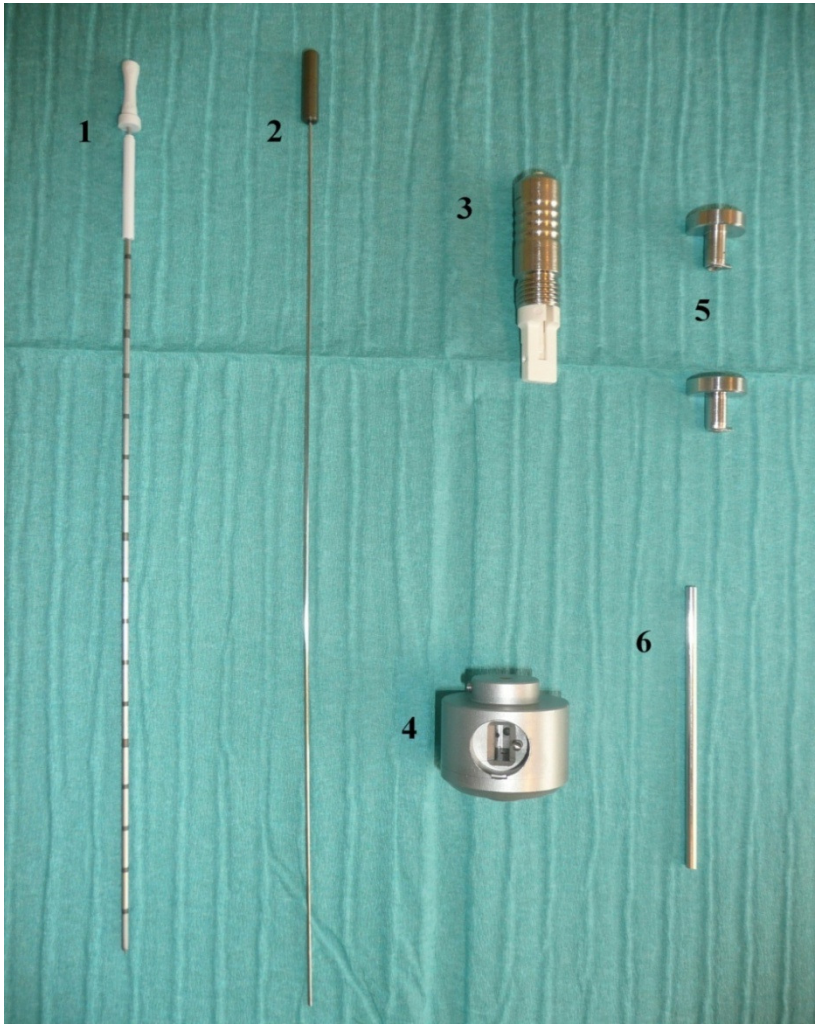
^{125}I localiseren in vivo

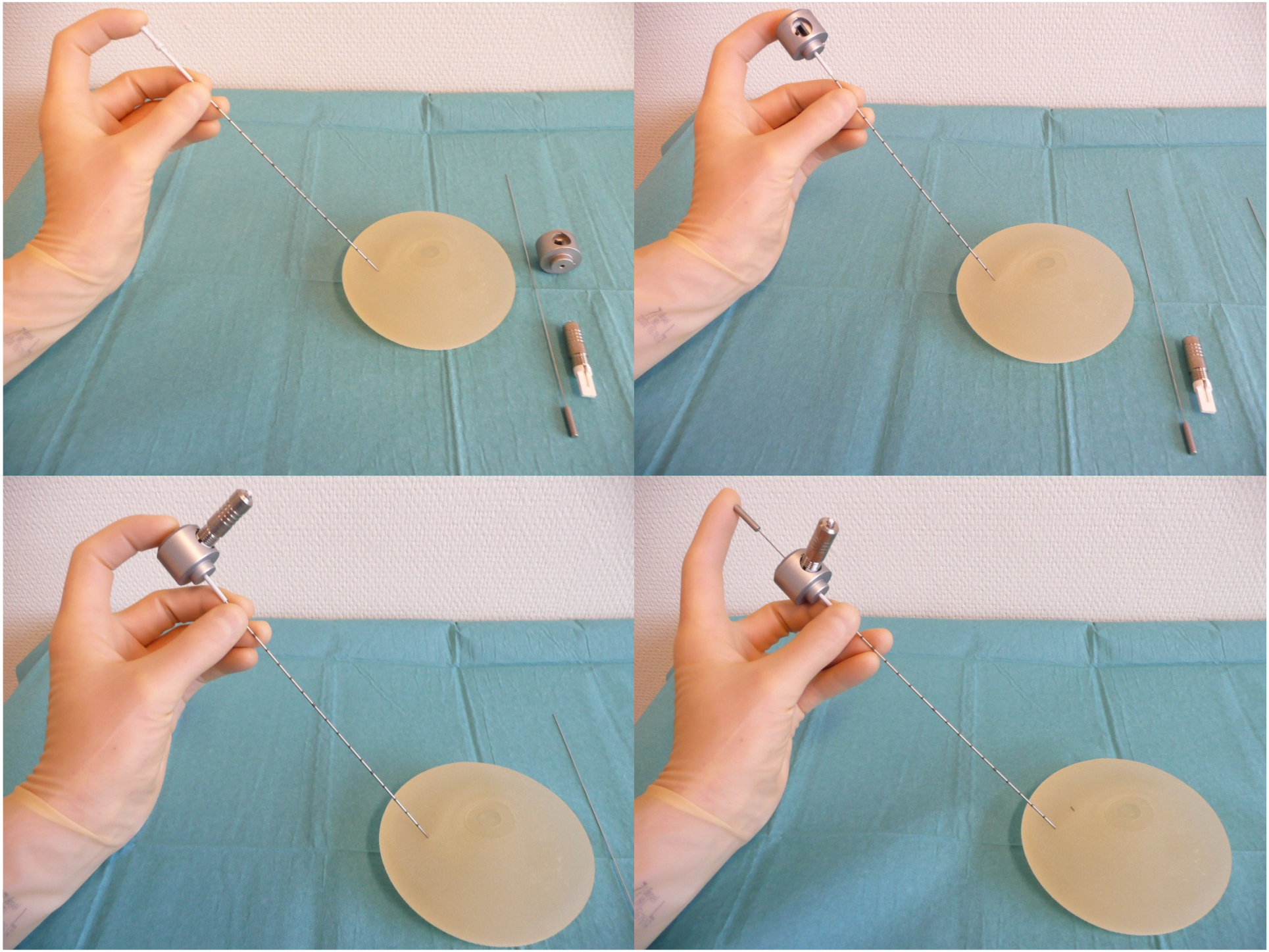
^{125}I en ^{99}Tc



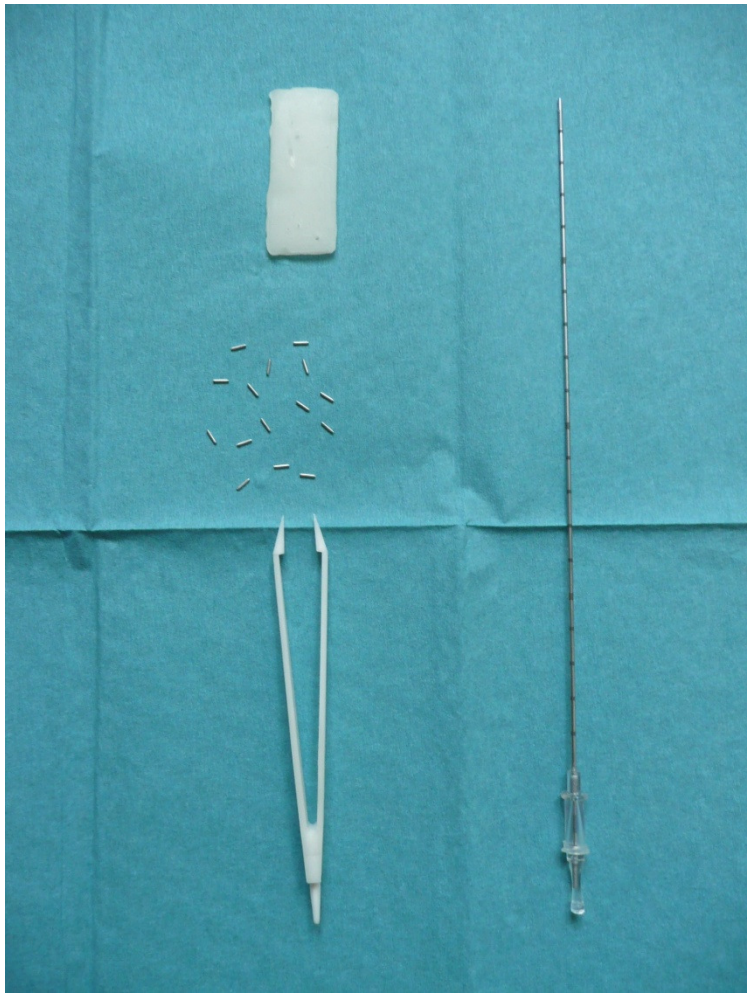
Neoprobe 2000

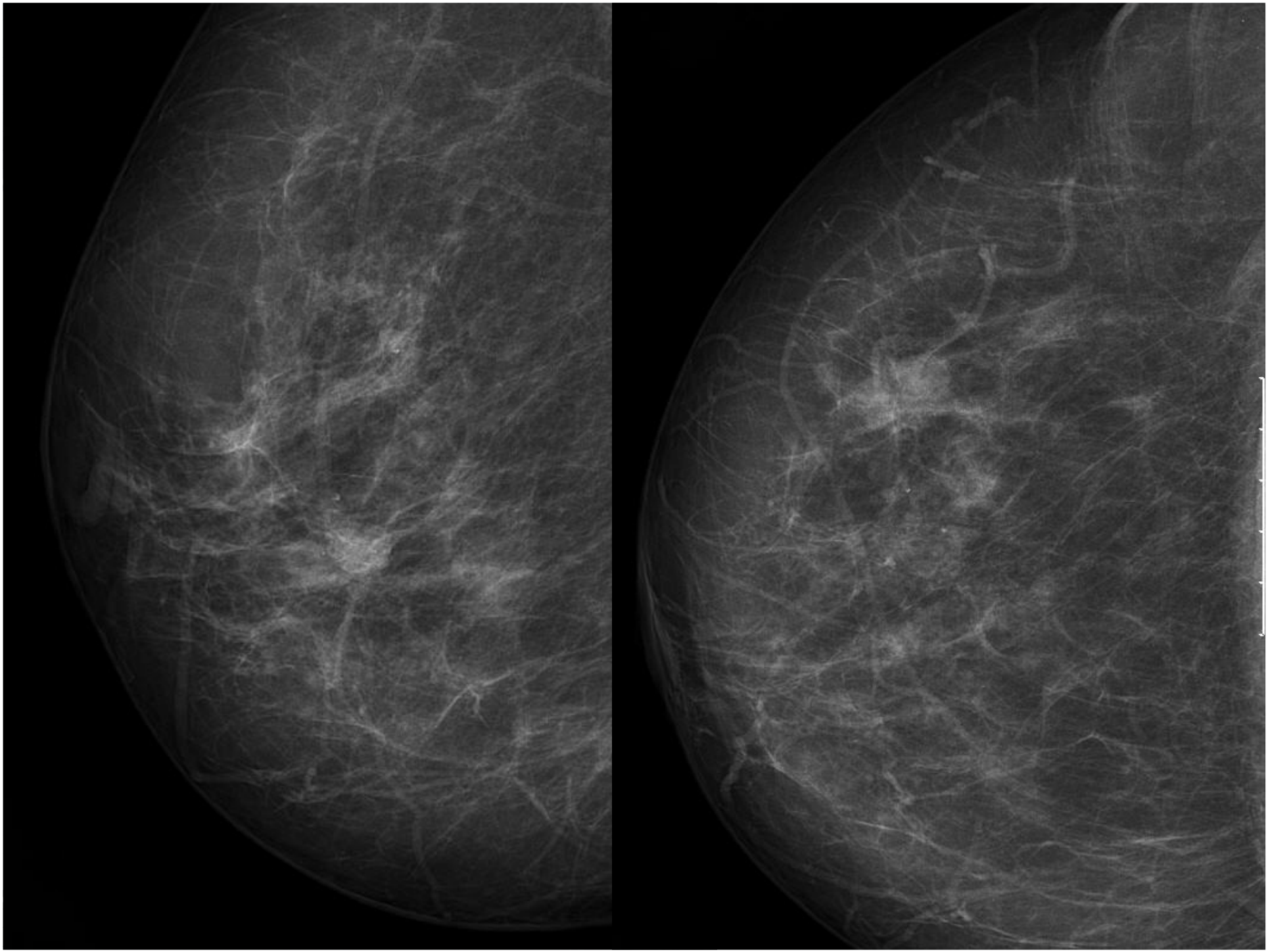
Benodigde introductiematerialen



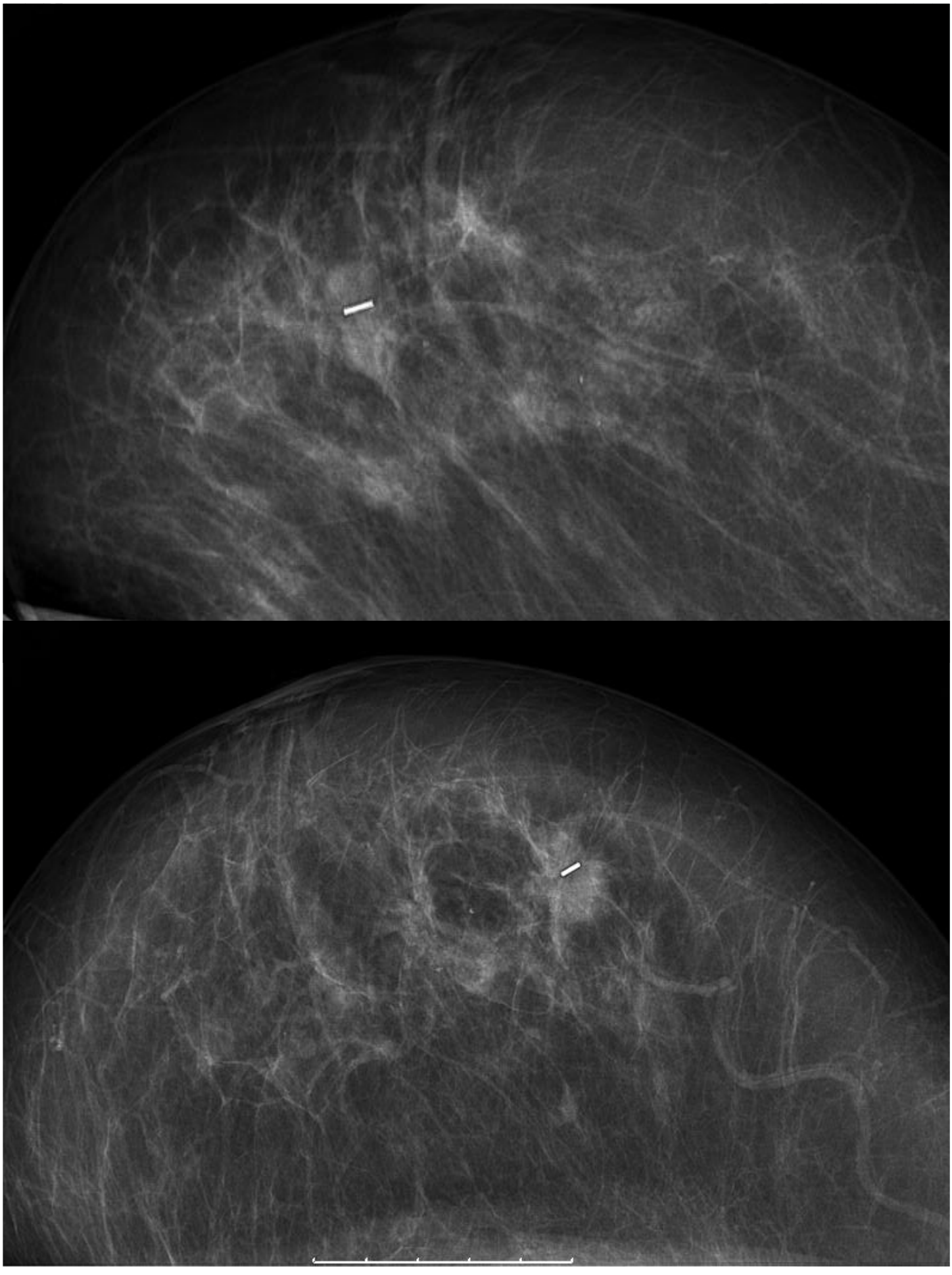


Benodigde introductiematerialen





Radiologische procedure

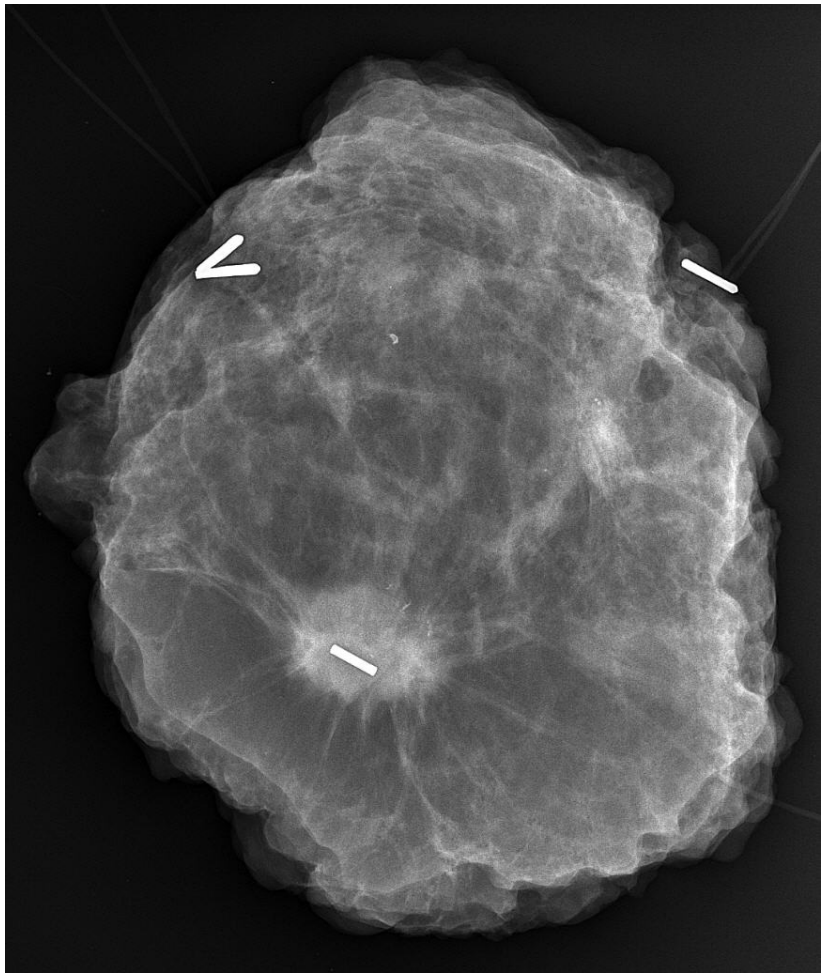


Chirurgische procedure

Techniek:

- **detectie I-125 zaadje met Neoprobe 2000 (gamma-probe)**
- **incisie huid**
- **verwijdering op geleide van detector**
- **continue monitoring**

Chirurgische procedure



Voordelen ^{125}I zaadje

- eenvoudige procedure, zowel voor radioloog als chirurg
- meest toegankelijke benadering voor radioloog, kortste weg voor de chirurg (oncoplastic surgery)
- repeterende localisatie (onderwijs)
- geen kans op dislocatie
- geen interferentie met de SN-procedure

Voordelen ^{125}I zaadje

- controleren op XMG

(observer onafhankelijk)

- meerdere zaadjes plaatsen

(microcalcificaties)

- verbeterde planning voor afdeling radiologie en chirurgie

Nadelen I-125 zaadje

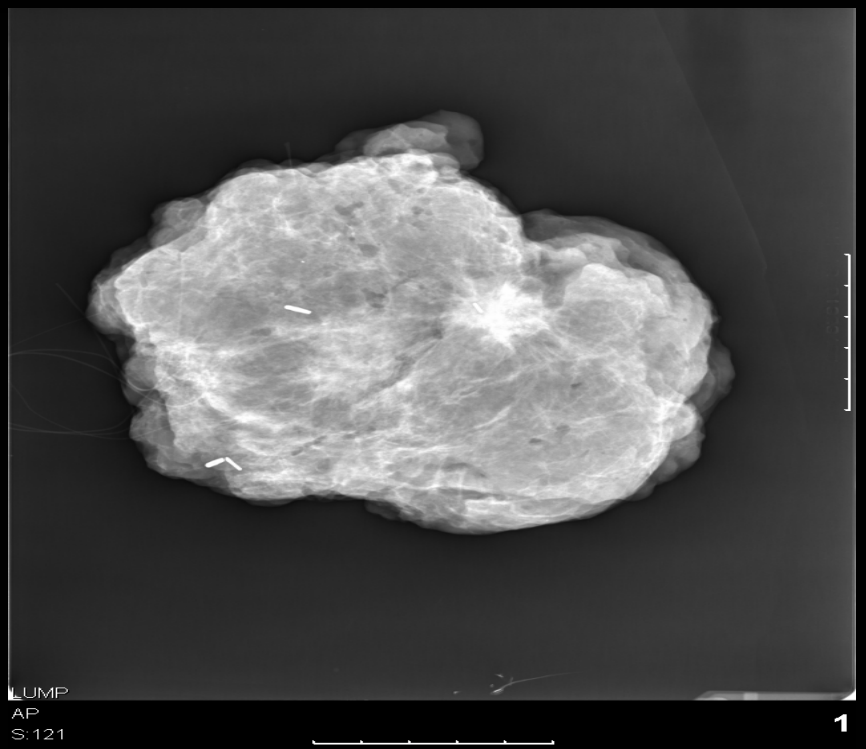
- zeer geringe stralingsdosis
- ieder ingebracht I-125 zaadje dient verwijderd te worden
- kan kwijtraken

CATHARINA-ZIEKENHUIS

125I zaadje zoek!?

CATHARINA-ZIEKENHUIS

125I zaadje zoek!?



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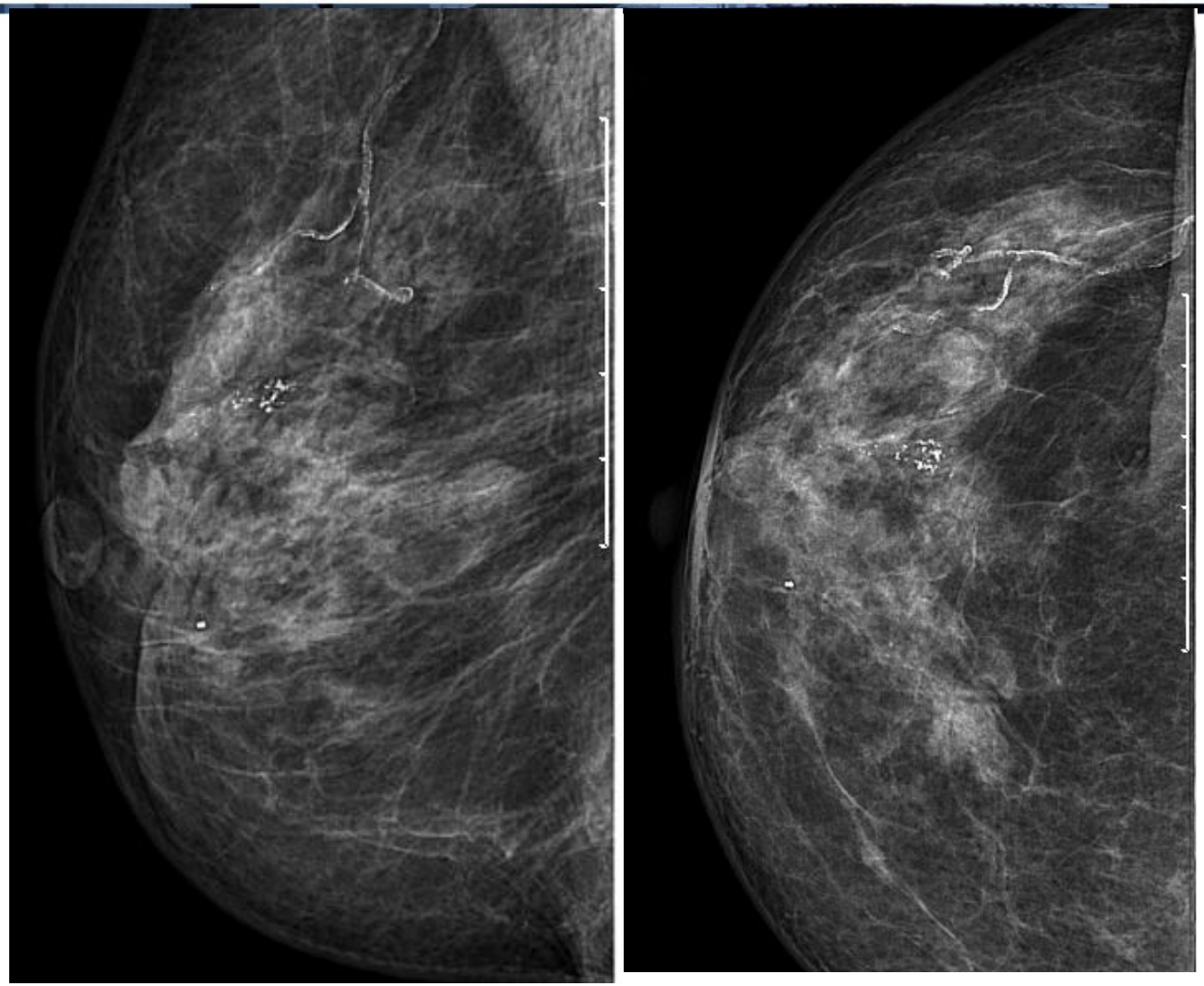

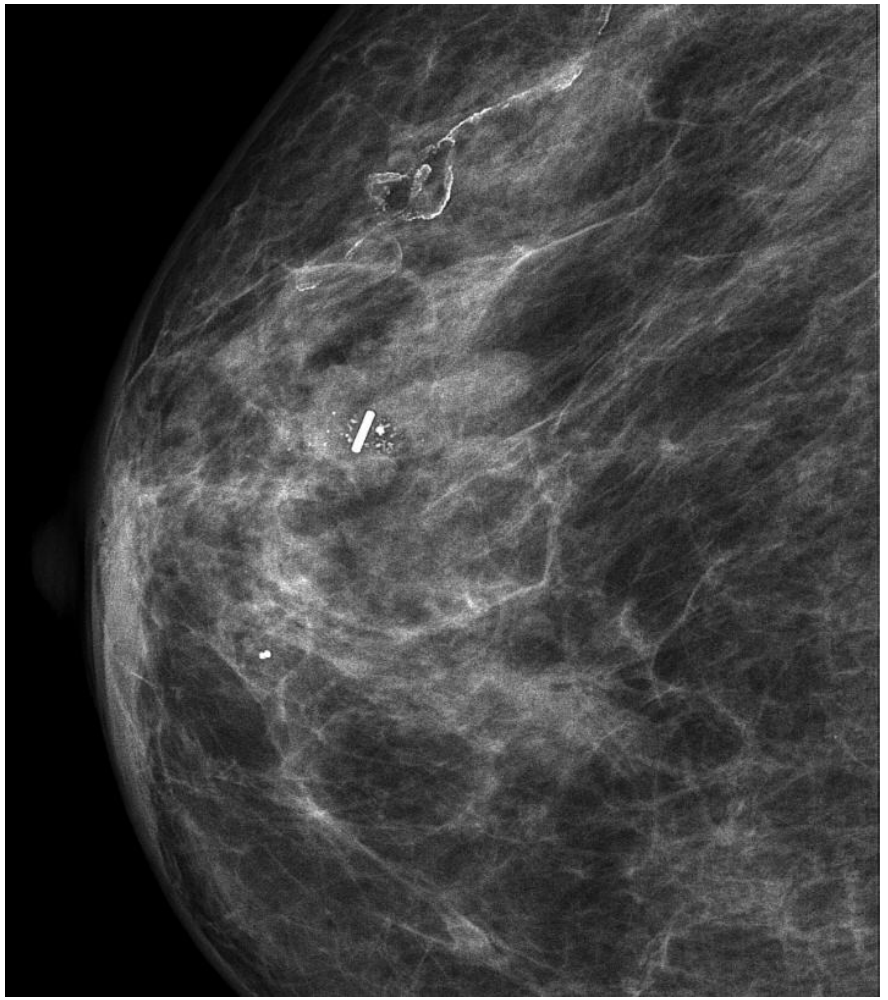

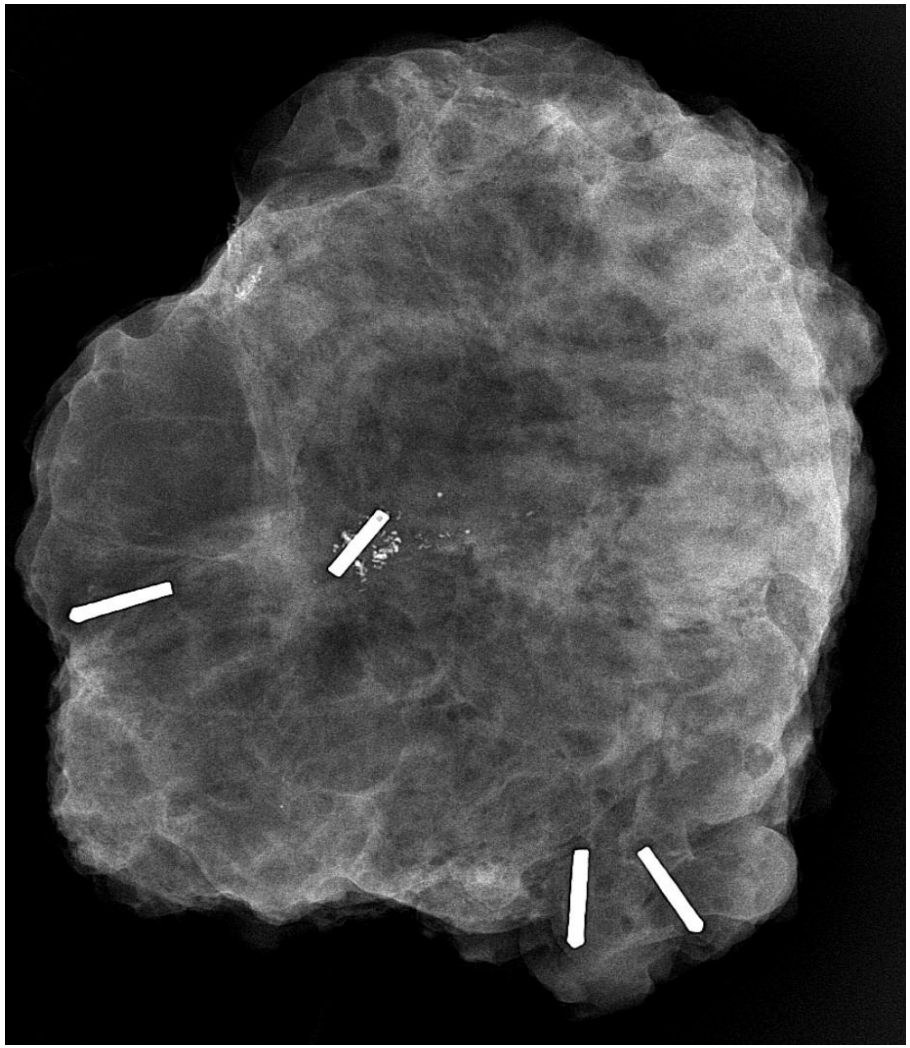

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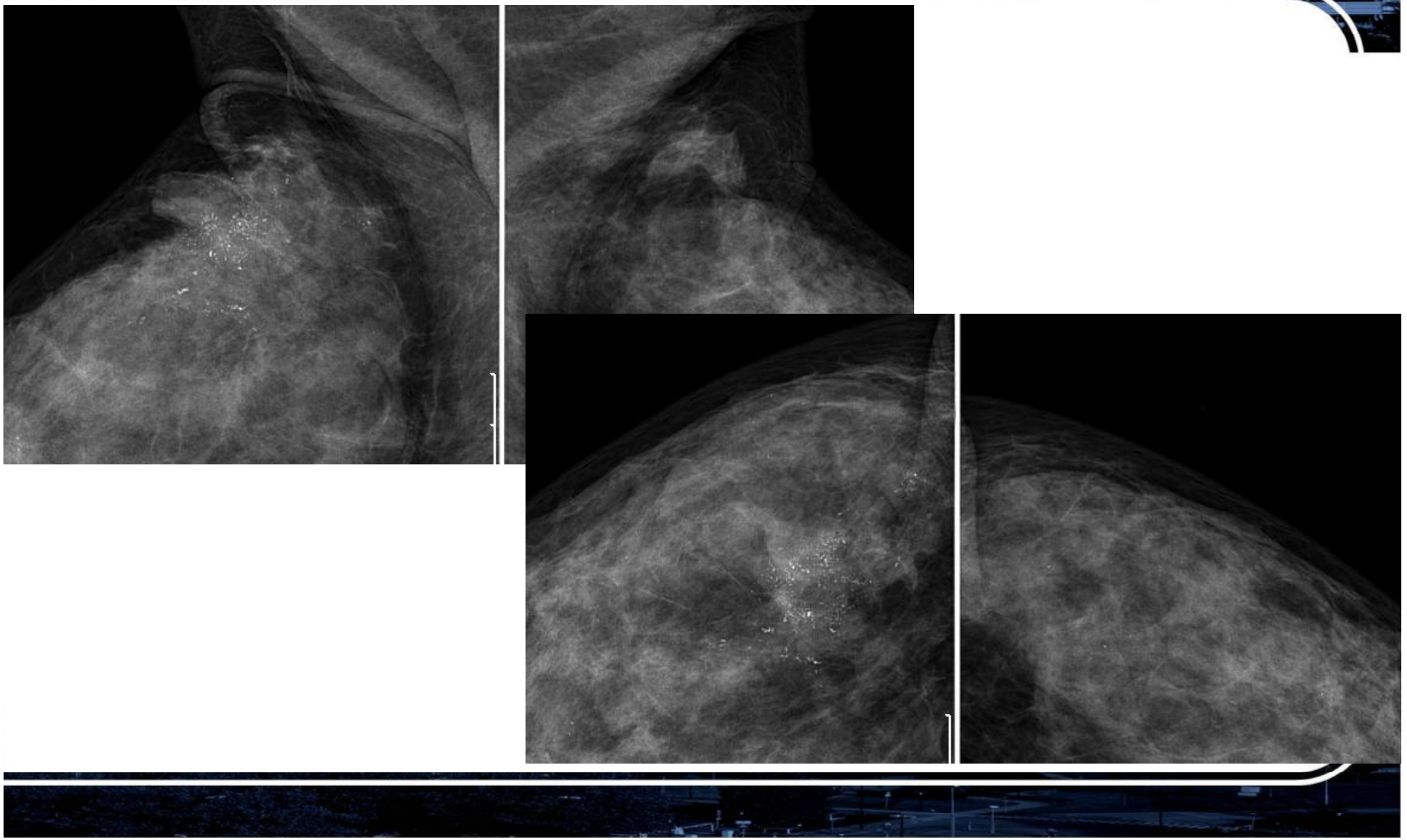

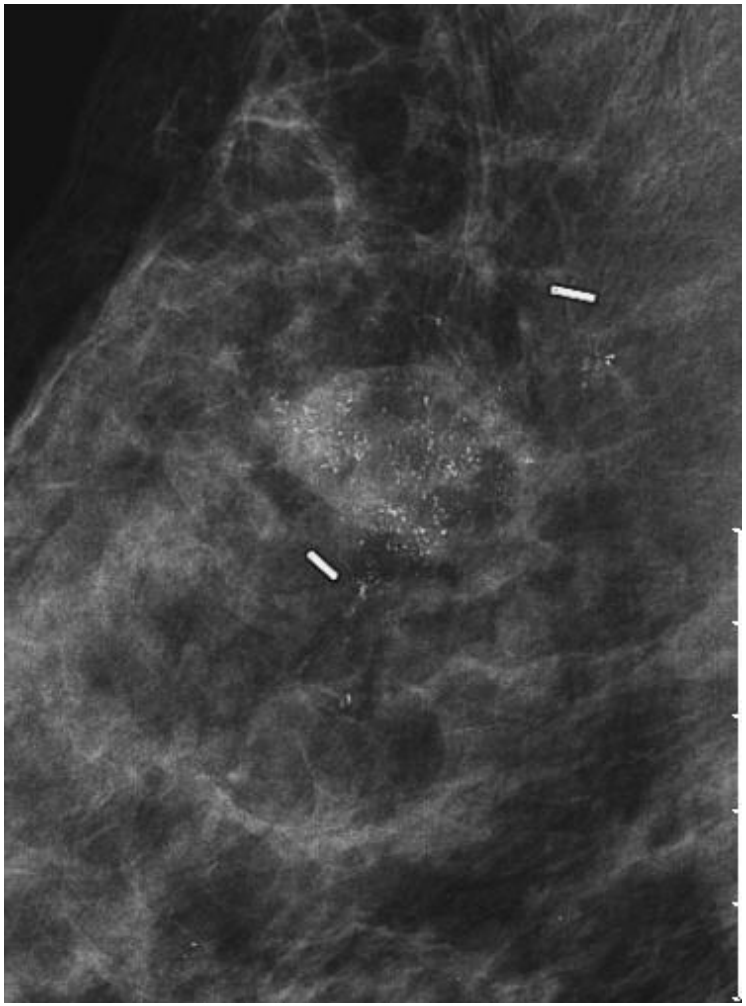

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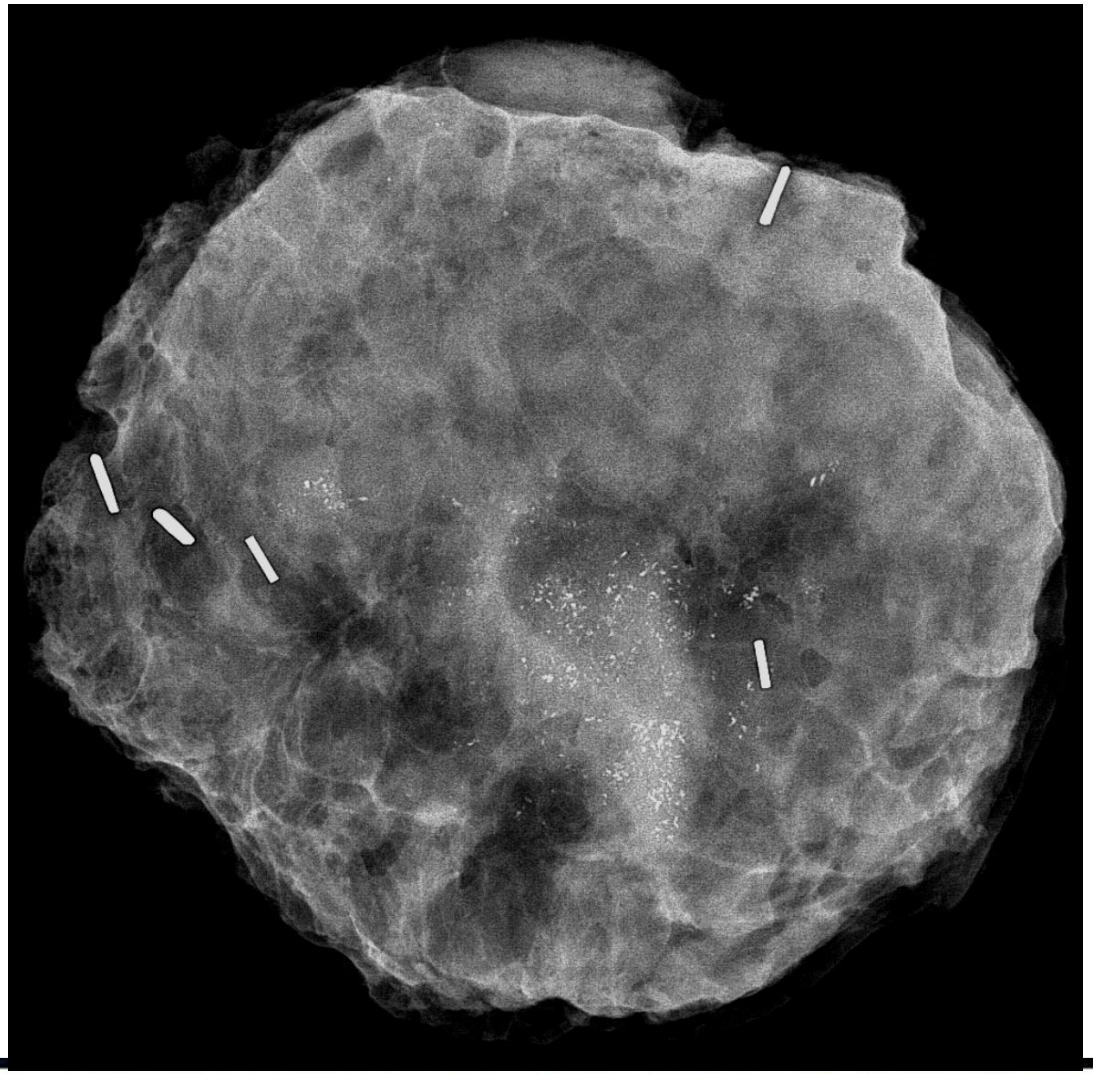

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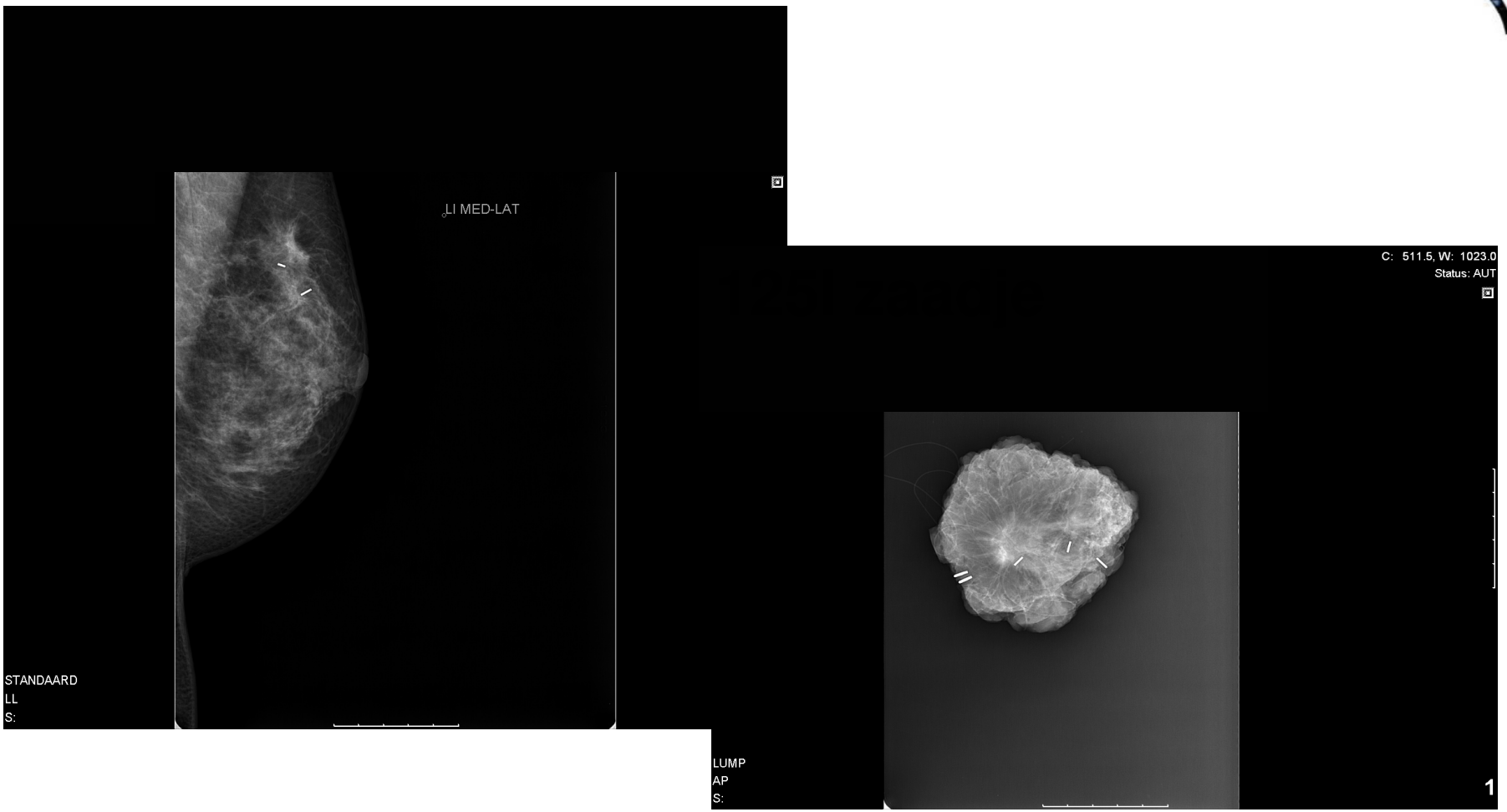
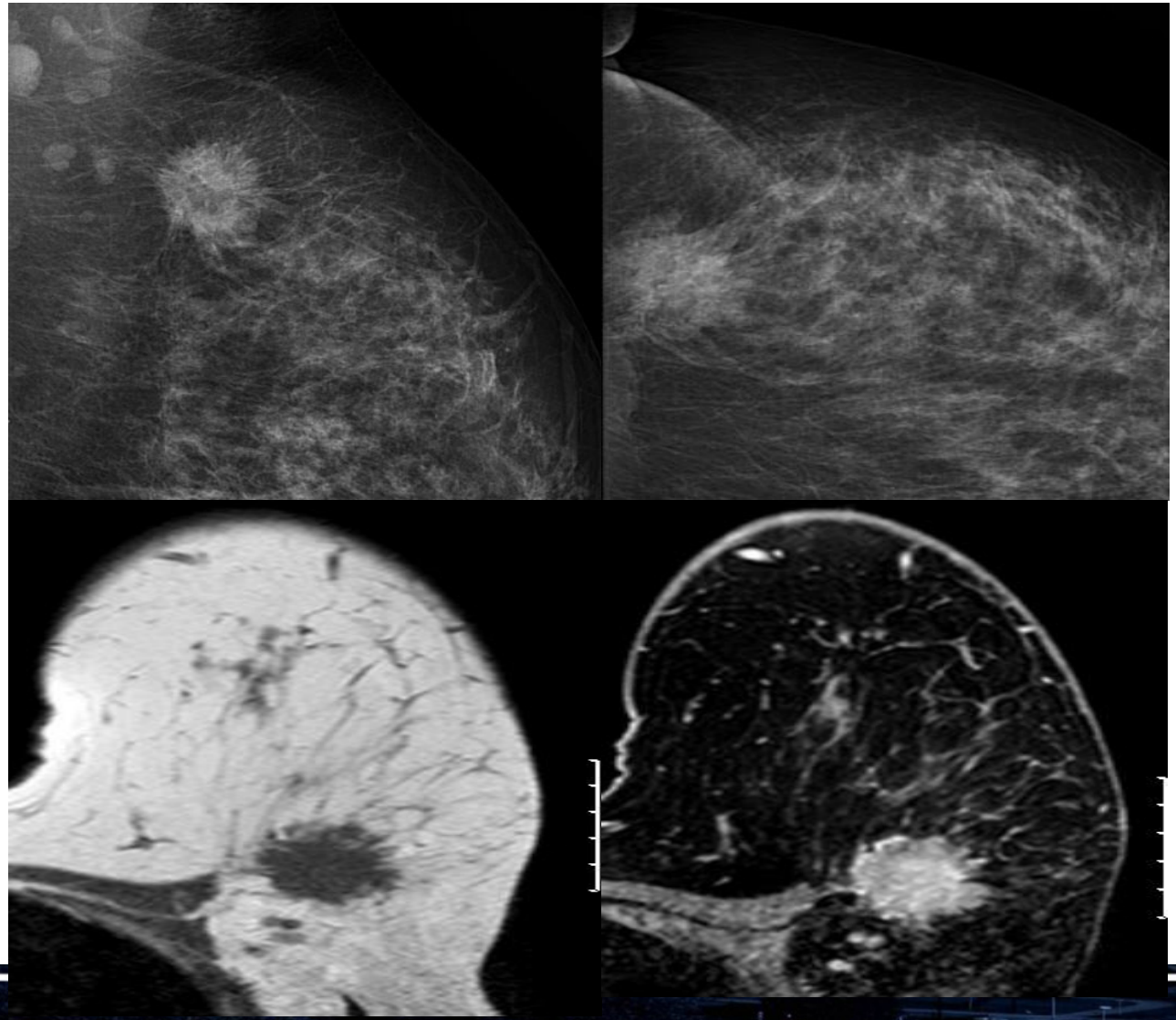


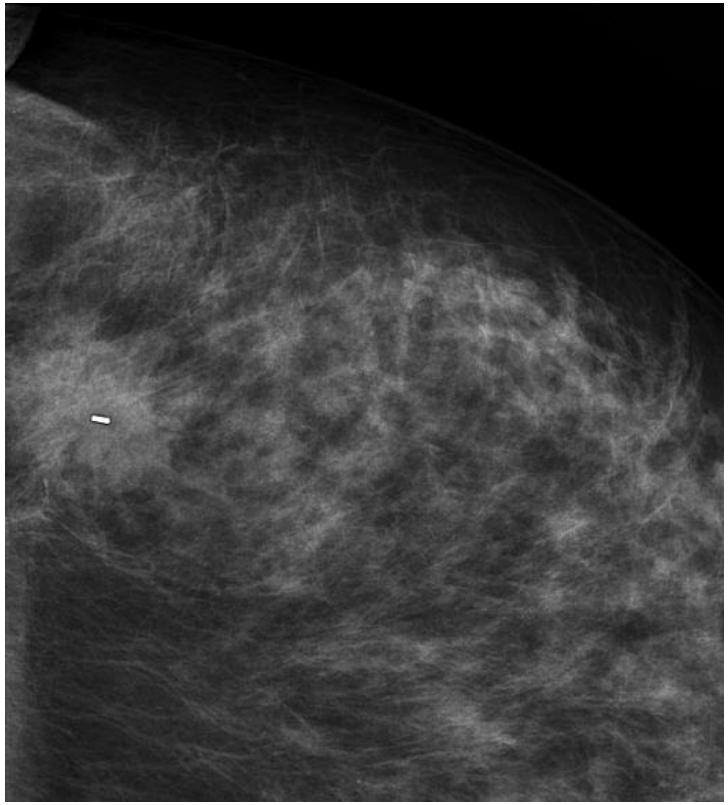
Neo-adjuvante chemotherapie

- Markeren tumoren met ^{125}I
- doel: tumorbed localisatie bij respons
- Voordeel: het bespaart de patient 1 procedure
- inmiddels standaard procedure in ons ZH

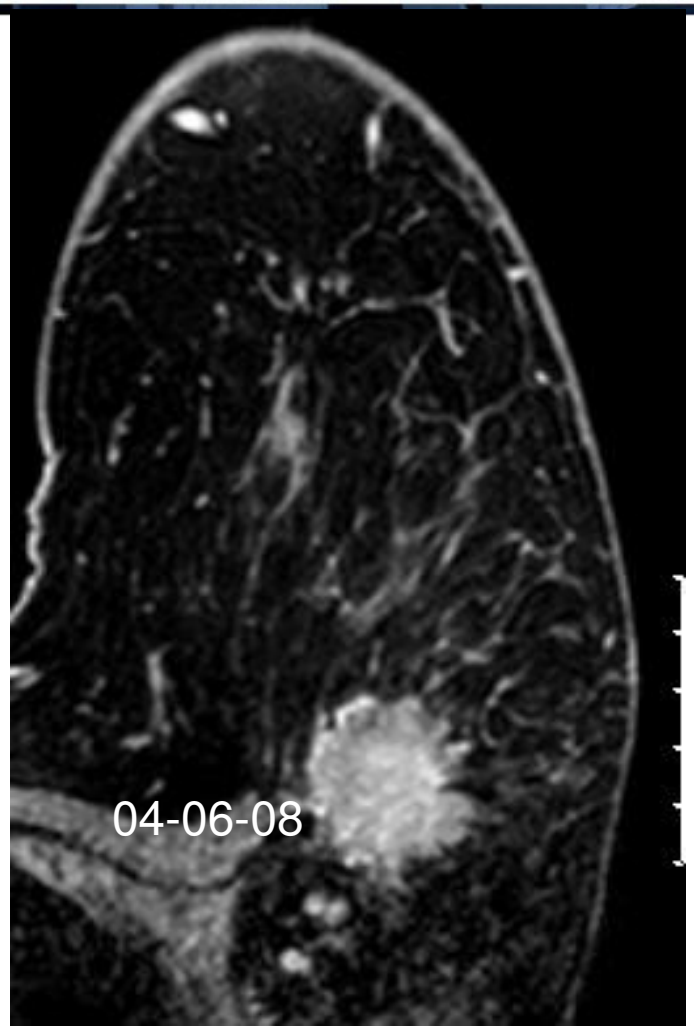
Neo-adjuvante chemotherapie

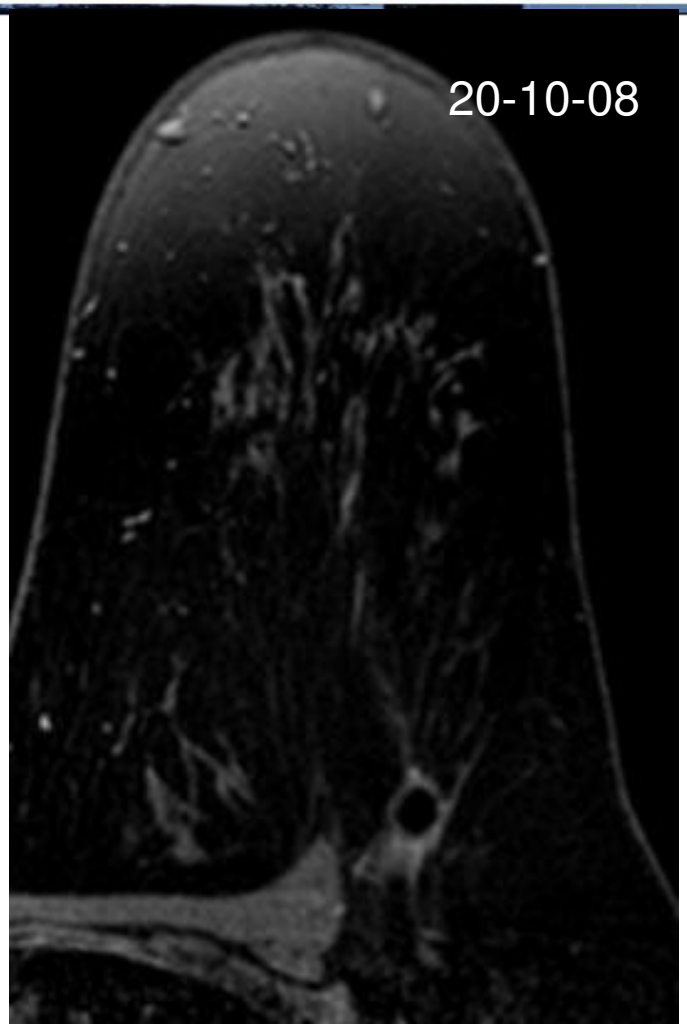


Neo-adjuvante chemotherapie



Neo-adjuvante chemotherapie

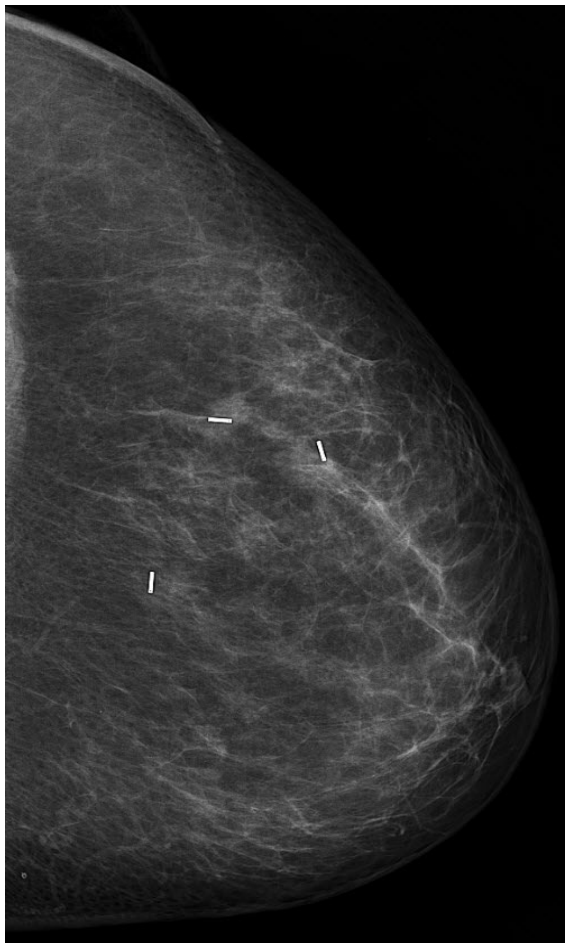




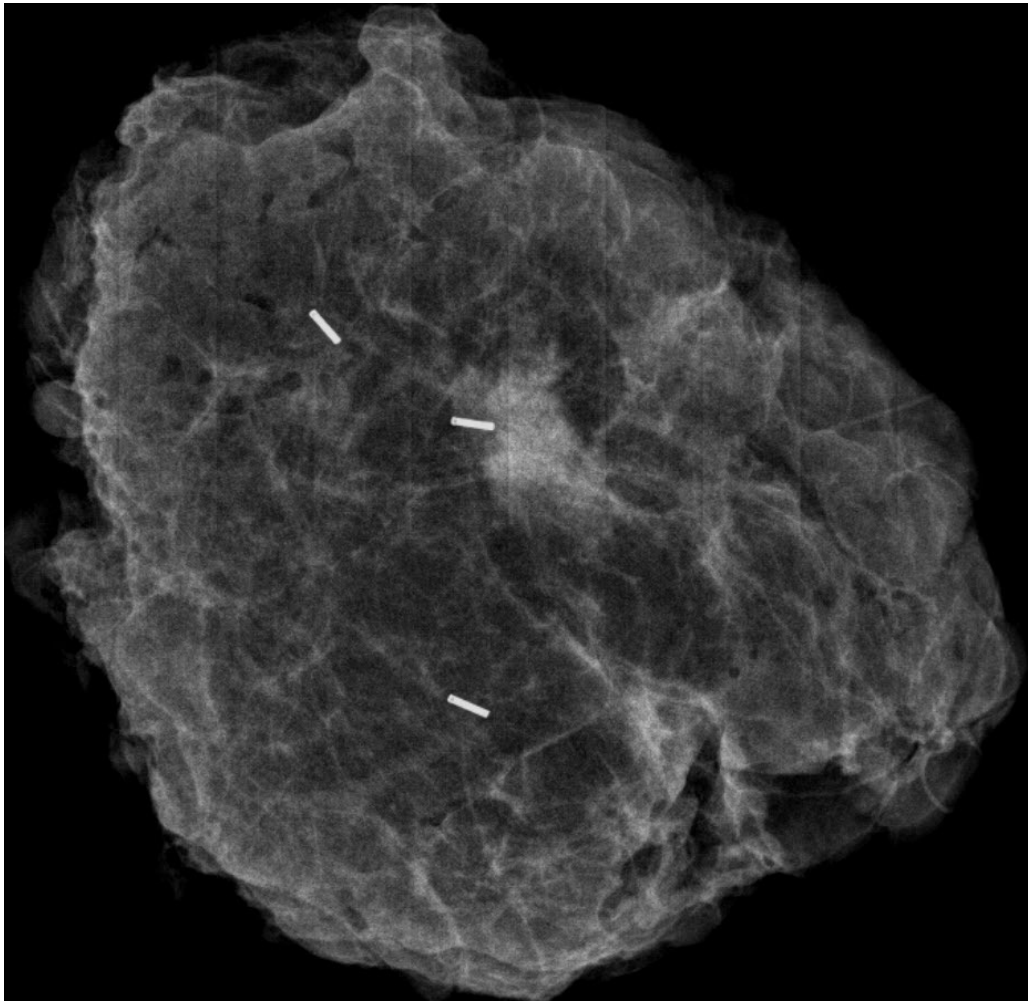
Neo-adjuvante chemotherapie

Neo-adjuvante chemotherapie

Neo-adjuvante chemotherapie



Neo-adjuvante chemotherapie



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Identification of residual breast tumour localization after neo-adjuvant chemotherapy using a radioactive 125 Iodine seed

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Abstract

Introduction: The use of neo-adjuvant chemotherapy has increased in the treatment of loco-regionally advanced primarily operable breast cancer. As a result of improved neo-adjuvant chemotherapy regimes the number of clinical as well as radiological responses have increased. In case of a complete response it is difficult to identify residual disease and to perform an adequate radical breast-conserving surgery. Therefore localization of the original tumour bed is mandatory. In this study we propose a novel technique with a seed containing radioactive 125 Iodine (^{125}I). The ^{125}I has a half-time of 60 days and is therefore still recognisable with a gamma probe after admittance of several courses of neo-adjuvant chemotherapy.
Material and Methods: In the period from July 2003 and November 2008, 47 consecutive patients had successful ^{125}I seed localization of a breast tumour before starting neo-adjuvant chemotherapy.
Results: The overall clinical response rate to neo-adjuvant chemotherapy was 100%. Complete clinical response occurred in 34 patients, partial clinical response occurred in 13 patients. Complete radiological response occurred in 18 patients, partial radiological response occurred in 29 patients. The initial surgical treatment consisted of breast-conserving surgery for all 47 patients, after a mean of 170 days (range: 70–220) after ^{125}I seed localization. In 19 patients pathology revealed no residual tumour, 23 patients showed a partial response. Only 3 lumpectomies were irradical.
Conclusion: This study has shown that ^{125}I seed localization is a novel and highly successful technique in localizing the tumour bed in patients who receive neo-adjuvant chemotherapy for breast cancer leading to a high percentage of radical margins in case of breast-conserving surgery.

Keywords: Breast cancer; Breast-conserving surgery; Neo-adjuvant chemotherapy; ^{125}I seed localization

Introduction

The treatment of patients with locally advanced as well as primary operable breast cancer has evolved to include neo-adjuvant chemotherapy strategies. Despite the fact that several randomized trials found little or no survival advantage comparing neo-adjuvant to adjuvant chemotherapy, neo-adjuvant chemotherapy does permit the assessment of the response of the primary tumour to a particular chemotherapy regimen [1–3]. Furthermore, neo-adjuvant chemotherapy substantially reduces the size of the primary tumour in a majority

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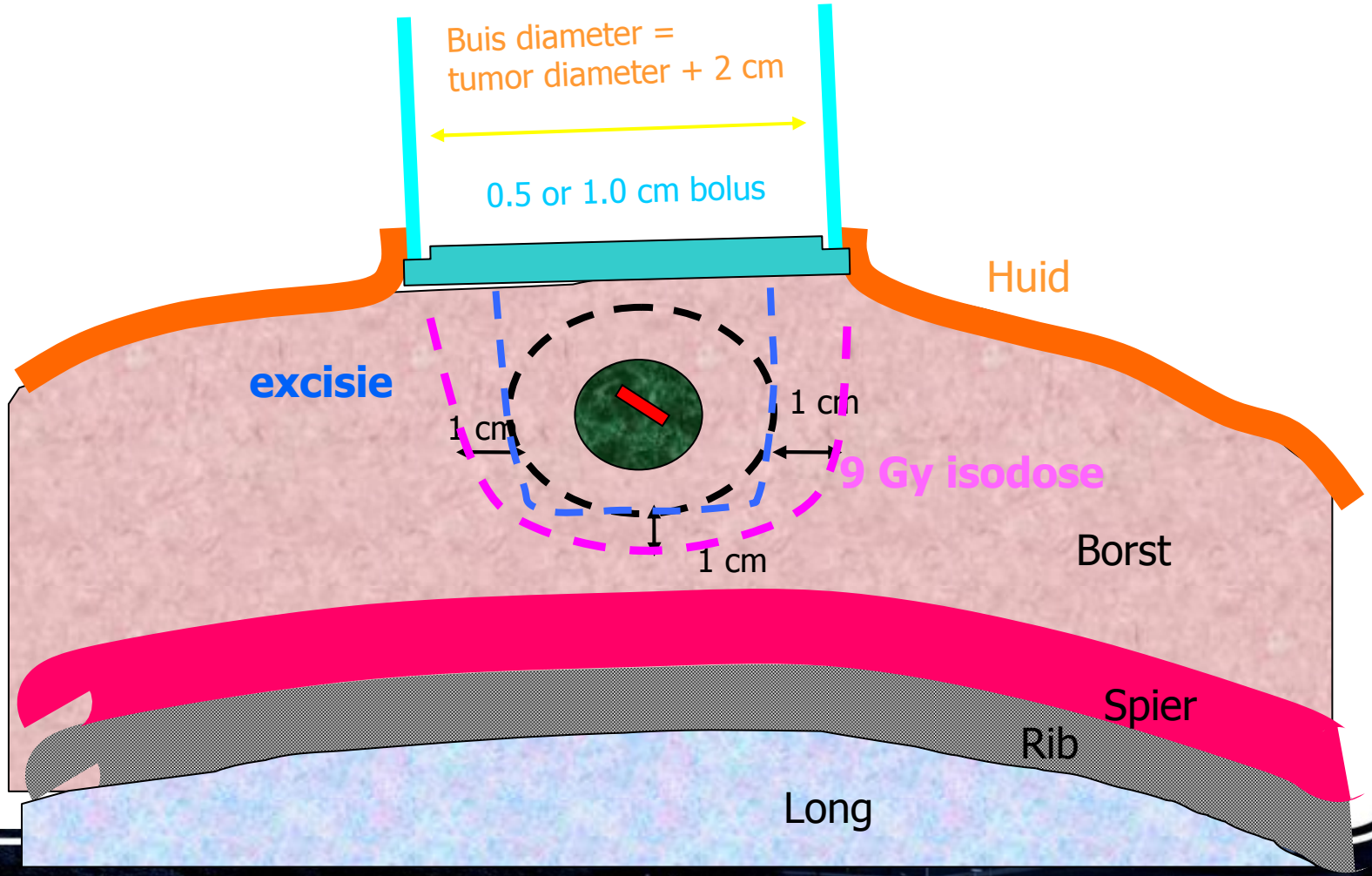
Intra-operatieve radiotherapie

- Intra –operatieve *in situ* boost (9Gy)
- ^{125}**I** zaadje = marker voor exacte
- bestraling op de OK, direct voorafgaande aan tumorexcisie

IORT: principe



Intra-operatieve radiotherapie

- **doel**: beperken huiddosis
  manipulatie tumor na radiotherapie
  kortere radiotherapie duur

- **pilot-studie**
  - n= 50 patienten
  - 2003-2007, mediane follow-up = 3,5 jaar
  - T1, > 0,5 cm thoraxwand en huid, > 50 jaar

Intra-operatieve radiotherapie

- **Operatie tijd**
  - 100 min (45-180 min)
- **Re-excisie i.v.m. irradicaliteit**
  - 2 pt'n (4%)
- **Cosmetisch resultaat**
  - Beter of vergelijkbaar met external beam boost (2 pt'n met ernstige fibrose)

Conclusies I-125 procedure

- elegante en eenvoudige techniek
- geen grote investering noodzakelijk
- Implementatie in ieder ziekenhuis
  (vergunning Kernenergiewet)
- laag irradicaliteits en re-excisie percentage

Conclusies vervolg

- spin-off: toepassing bij neo-adjuvante chemotherapie en intra-operatieve radiothe-rapie (IORT)
- belangrijke positieve bijdrage aan de mamma-oncologische zorg