CARCINOMA DE MAMA

Es la neoplasia más frecuente en la mujer
y la principal causa de muerte femenina

73,7 / 100.000
1 de cada 9 en España
1 de cada 20 en el mundo

CARCINOMA DE MAMA

Factores de riesgo

GENÉTICOS Y FAMILIARES

CM ESPORÁDICO

65-70%
Sin antecedentes en 2 ó más generaciones

CM FAMILIAR

20-30%
1 ó más familiares de 1° ó 2° grado
No ligado a mutaciones genéticas

CM HEREDITARIO

Autosómica dominante
5-10%
Antec. fam. de Ca mama y otros relacionados
Bilateral
Edad temprana
Mutación genes supresores BRCA 1 y 2

CARCINOMA DE MAMA

Factores de riesgo

Sexuales y hormonales

SEXO Mujeres 99%

Hombres 1%

EDAD Aumenta durante los años de actividad hormonal sexual

CICLO MENSTRUAL CORTO Más riesgo

MENARQUIA Menarquia precoz y menopausia tardía

PARIDAD Nulíparas > riesgo

1er embarazo > 35 años ↑ riesgo

LACTANCIA Lactancias > 6 meses protegen

HORMONAS EXÓGENAS THS > 5 años aumenta 30-45% riesgo

ANTICONCEPTIVOS ORALES ????

CARCINOMA DE MAMA

Factores de riesgo

Dietéticos

- Consumo de grasa animal
- Alcohol
- Obesidad

Ambientales

- Radiaciones ionizantes
- Tabaco
- Estatus socioeconómico alto

Enf. Benignas de la mama

- Lesiones benignas no proliferativas
- Lesiones benignas proliferativas
- Hiperplasia epitelial atípica

Antecedentes de cáncer

- Ca de mama previo x 3-5
- Ca de endometrio, ovario, colon

CARCINOMA DE MAMA

Prevención

Primaria

- Evitar exposición a factores de riesgo (obesidad, THS, Rx...)
- Consumir Vit. A y derivados
- Lactancia
- Actividad física

BRCA:
- 2 ó + antec. 1º grado
- Antec. 1º grado bilat.
- Antec. 1º grado premenop.

Secundaria

Diagnóstico precoz
- Autoexploración
- Examen clínico
- Screening (anual < 50; bienal > 50 años)

Seguimiento estricto mujeres de riesgo

Terciaria

Reducir o paliar secuelas
- Linfedema
- Reconstrucción postmastectomía
- Apoyo psicológico

CARCINOMA DE MAMA

CARCINOMA IN SITU

Ca DUCTAL IN SITU (CDIS) 80%

- Comedocarcinoma
- Sólido
- Cribiforme
- Papilar
- Micropapilar

Ca LOBULILLAR IN SITU (CLIS)

- Bilateralidad 50-75%
- Multicentricidad 50%

Marcador de riesgo de Ca infiltrante → 25-30% lo padecerán

CARCINOMA DE MAMA

CARCINOMA INFILTRANTE

Ca DUCTAL INFILTRANTE: 75%, sólido, corte característico.

Ca LOBULILLAR INFILTRANTE: 10%, bilateral 30%, multicéntrico.

Ca MEDULAR: < 10%, en jóvenes.

Ca COLOIDE O MUCINOSO: 2%, mujeres mayores.

Ca TUBULAR: 2%, jóvenes, multifocal, bilateral.

Ca PAPILAR INFILTRANTE: < 2%

ENF. DE PAGET: 2%, 2/3 intraductal, 1/3 infiltrante.

CARCINOMA DE MAMA

SARCOMAS

Liposarcoma, leiomiosarcoma, fibrosarcoma, angiosarcoma

CISTOSARCOMA PHYLLODES

0,5 %
Grandes: 6-8 cm.
Delimitados
Móviles
Benignos / Borderline / Malignos

Estadificación

Staging

Table 1

American Joint Committee on Cancer (AJCC)
TNM Staging System For Breast Cancer

Primary Tumor (T)

Definitions for classifying the primary tumor (T) are the same for clinical and for pathologic classification. If the measurement is made by the physical examination, the examiner will use the major headings (T1, T2, or T3). If other measurements, such as mammographic or pathologic measurements, are used, the subsets of T1 can be used. Tumors should be measured to the nearest 0.1 cm increment.

TX		Primary tumor cannot be assessed
T0		No evidence of primary tumor
Tis		Carcinoma in situ
Tis (DCIS)		Ductal carcinoma in situ
Tis (LCIS)		Lobular carcinoma in situ
Tis (Paget's)		Paget's disease of the nipple with no tumor

Note: Paget's disease associated with a tumor is classified according to the size of the tumor.

T1		Tumor 2 cm or less in greatest dimension
	T1mic	Microinvasion 0.1 cm or less in greatest dimension
	T1a	Tumor more than 0.1 cm but not more than 0.5 cm in greatest dimension
	T1b	Tumor more than 0.5 cm but not more than 1 cm in greatest dimension
	T1c	Tumor more than 1 cm but not more than 2 cm in greatest dimension
T2		Tumor more than 2 cm but not more than 5 cm in greatest dimension
T3		Tumor more than 5 cm in greatest dimension
T4		Tumor of any size with direct extension to (a) chest wall or (b) skin, only as described below
	T4a	Extension to chest wall, not including pectoralis muscle
	T4b	Edema (including peau d'orange) or ulceration of the skin of the breast, or satellite skin nodules confined to the same breast
	T4c	Both T4a and T4b
	T4d	Inflammatory carcinoma

Regional Lymph Nodes (N)

Clinical

NX		Regional lymph nodes cannot be assessed (e.g., previously removed)
N0		No regional lymph node metastasis
N1		Metastasis to movable ipsilateral axillary lymph node(s)
N2		Metastases in ipsilateral axillary lymph nodes fixed or matted, or in *clinically apparent** ipsilateral internal mammary nodes in the *absence* of clinically evident axillary lymph node metastasis
	N2a	Metastases in ipsilateral axillary lymph nodes fixed to one another (matted) or to other structures
	N2b	Metastasis only in *clinically apparent** ipsilateral internal mammary nodes and in the *absence* of clinically evident axillary lymph node metastasis
N3		Metastasis in ipsilateral infraclavicular lymph node(s) with or without axillary lymph node involvement, or in *clinically apparent** ipsilateral internal mammary lymph node(s) and in the *presence* of clinically evident axillary lymph node metastasis; or metastasis in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement
	N3a	Metastasis in ipsilateral infraclavicular lymph node(s)
	N3b	Metastasis in ipsilateral internal mammary lymph node(s) and axillary lymph node(s)
	N3c	Metastasis in ipsilateral supraclavicular lymph node(s)

**Clinically apparent* is defined as detected by imaging studies (excluding lymphoscintigraphy) or by clinical examination or grossly visible pathologically.

Staging continued on next page (ST-2)

Estadificación 2

Table 1 (continued)

Distant Metastasis (M)

MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

STAGE GROUPING

Stage 0	Tis	N0	M0
Stage I	T1*	N0	M0
Stage IIA	T0	N1	M0
	T1*	N1	M0
	T2	N0	M0
Stage IIB	T2	N1	M0
	T3	N0	M0
Stage IIIA	T0	N2	M0
	T1*	N2	M0
	T2	N2	M0
	T3	N1	M0
	T3	N2	M0
Stage IIIB	T4	N0	M0
	T4	N1	M0
	T4	N2	M0
Stage IIIC	Any T	N3	M0
Stage IV	Any T	Any N	M1

* T1 includes T1mic

Note: Stage designation may be changed if post-surgical imaging studies reveal the presence of distant metastases, provided that the studies are carried out within 4 months of diagnosis in the absence of disease progression and provided that the patient has not received neoadjuvant therapy.

HISTOPATHOLOGIC TYPE

The histopathologic types are the following:

In situ Carcinomas

NOS (not otherwise specified)
Intraductal
Paget's disease and intraductal

Invasive Carcinomas

NOS
Ductal
Inflammatory
Medullary, NOS
Medullary with lymphoid stroma
Mucinous
Papillary (predominantly micropapillary pattern)
Tubular
Lobular
Paget's disease and infiltrating
Undifferentiated
Squamous cell
Adenoid cystic
Secretory
Cribriform

HISTOPATHOLOGIC GRADE (G)

All invasive breast carcinomas with the exception of medullary carcinoma should be graded. The Nottingham combined histologic grade (Elston-Ellis modification of Scarff-Bloom-Richardson grading system) is recommended.[1,2] The grade for a tumor is determined by assessing morphologic features (tubule formation, nuclear pleomorphism, and mitotic count), assigning a value of 1 (favorable) to 3 (unfavorable) for each feature, and adding together the scores for all three categories. A combined score of 3-5 points is grade 1; a combined score of 6-7 points is grade 2; a combined score of 8-9 points is grade 3.

[1] Elston CW, Ellis IO. Pathological prognostic factors in breast cancer. I. The value of histologic grade in breast cancer: experience from a large study with long-term follow-up. Histopathology 1991;19:403-410.

[2] Fitzgibbons PL, Page DL, Weaver D et al. Prognostic factors in breast cancer. College of American Pathologists consensus statement 1999. Arch Pathol Lab Med 2000;124:966-978.

HISTOLOGIC GRADE (NOTTINGHAM COMBINED HISTOLOGIC GRADE IS RECOMMENDED)

GX	Grade cannot be assessed
G1	Low combined histologic grade (favorable)
G2	Intermediate combined histologic grade (moderately favorable)
G3	High combined histologic grade (unfavorable)

CARCINOMA DE MAMA

CLÍNICA

DOLOR: tipo, inicio, cíclico, irradiación.

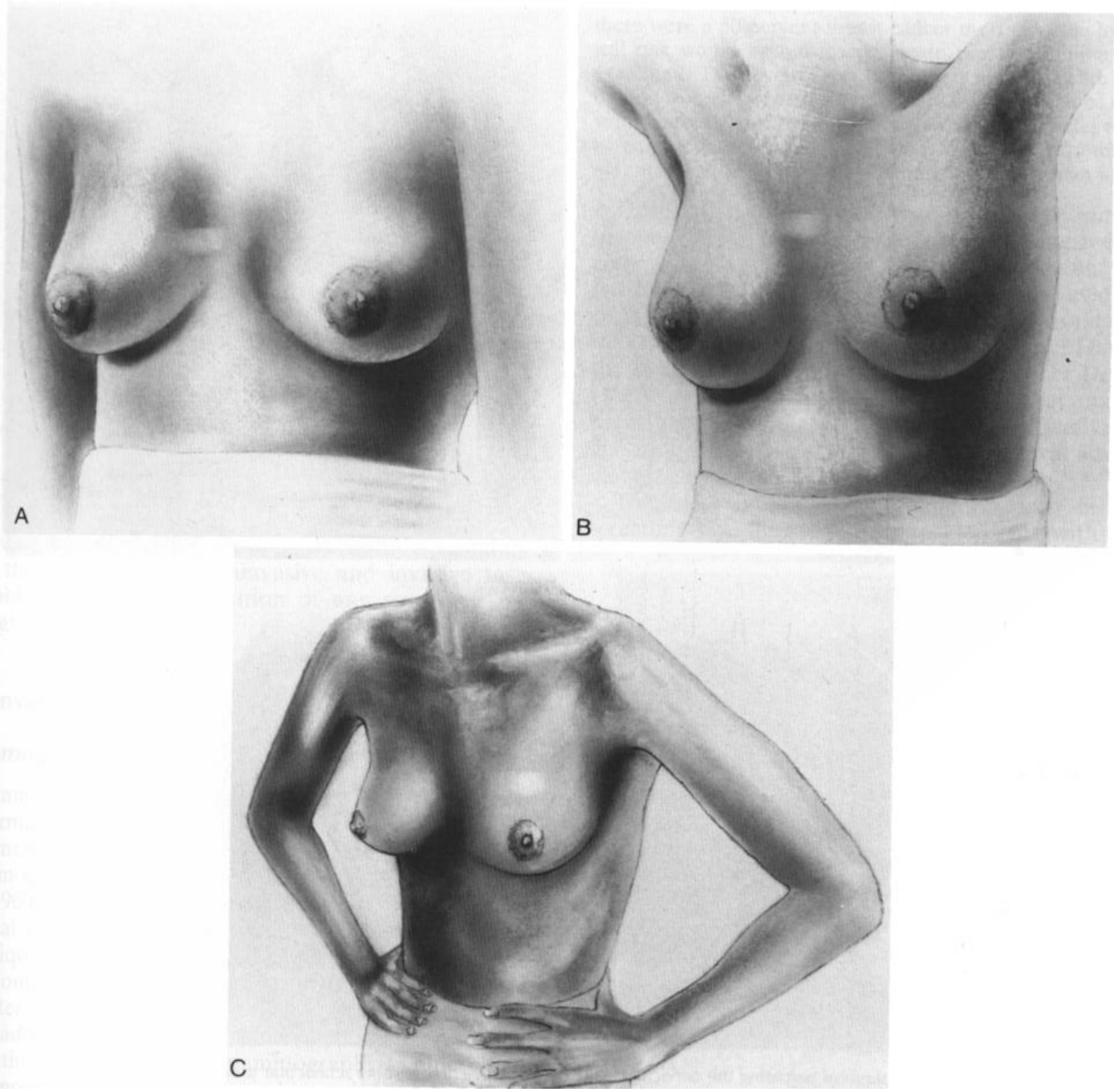
CAMBIOS DE TAMAÑO MAMARIO: asimetrías, ginecomastia.

PEZÓN: retracción, eczema, secreción (aspecto, lateralidad, orificio)

TUMOR: consistencia, bordes, movilidad.

PIEL: retracción, enrojecimiento, "piel de naranja".

GANGLIOS: axilares, supraclaviculares.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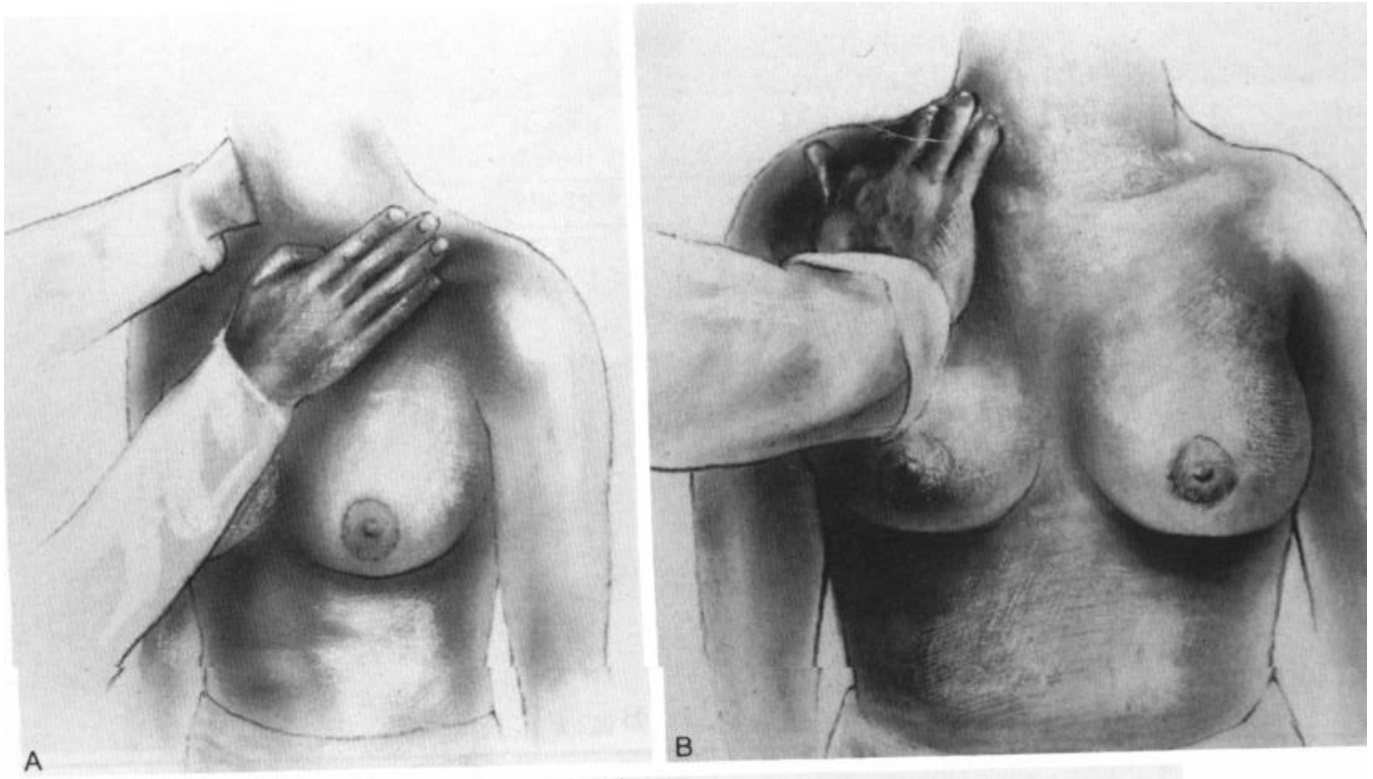
B
C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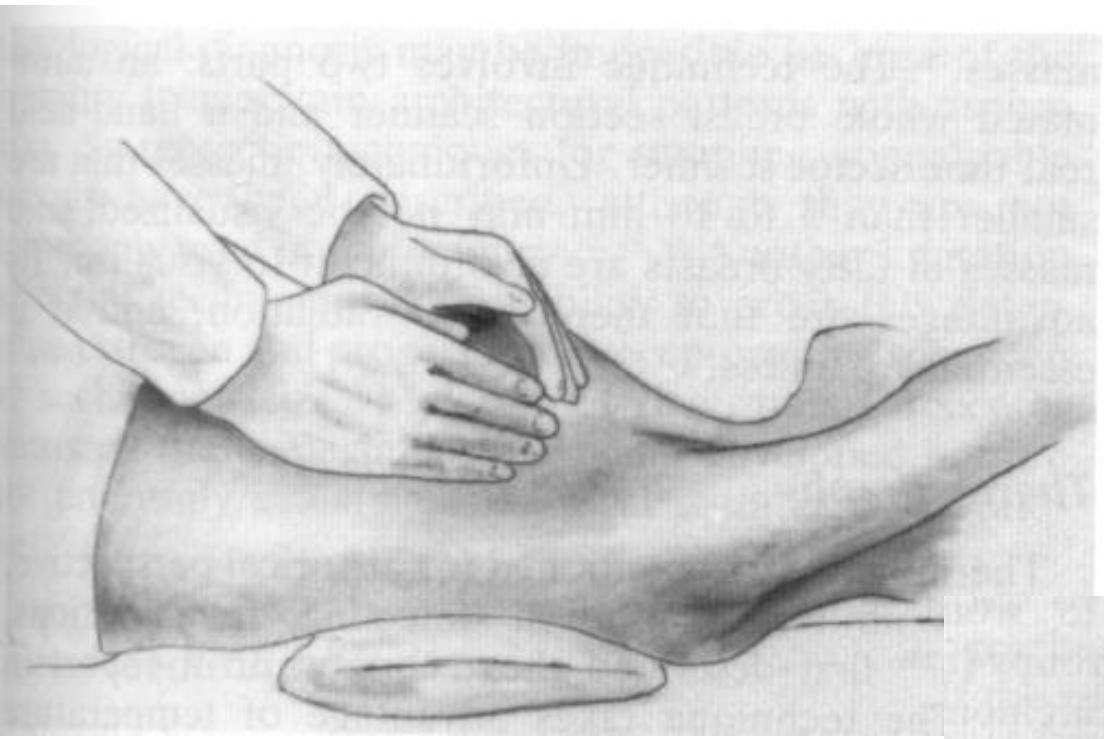

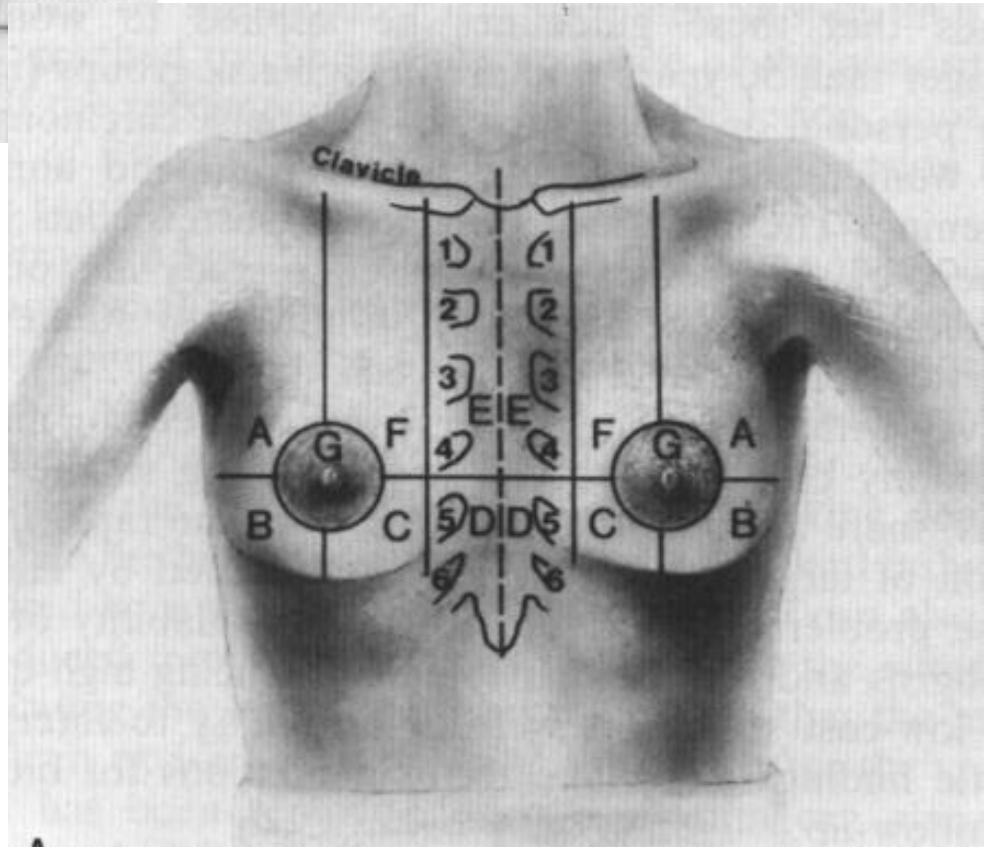
Clavicle
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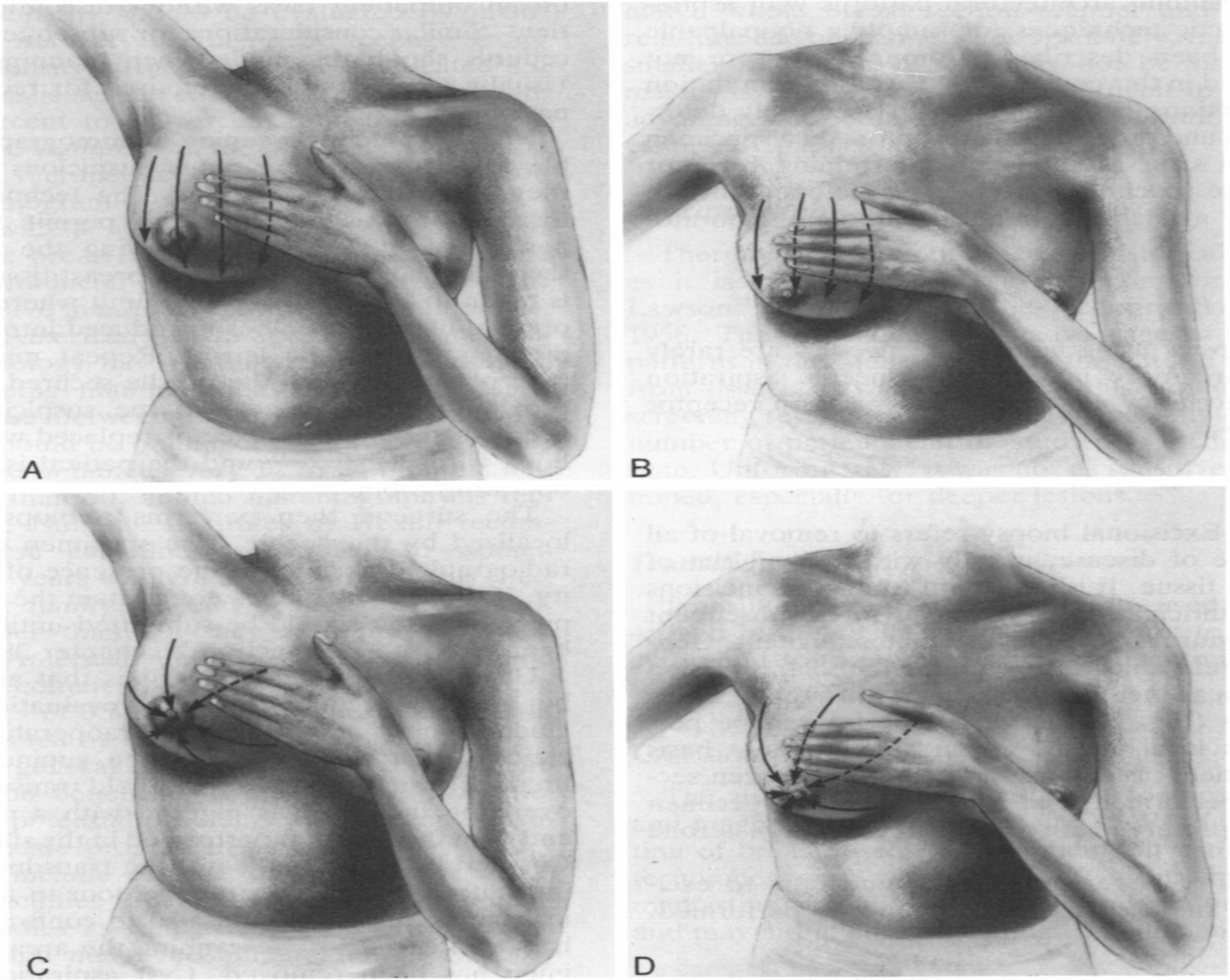

A
B
C
D

CARCINOMA DE MAMA

PRONÓSTICO

Factores clínicos

Edad: peor en < 35 años

Sexo: peor en hombres

Estado menopáusico

Estado general

Intervalo libre de enfermedad

CARCINOMA DE MAMA

PRONÓSTICO

Factores anatomopatológicos

Ganglios afectados (Mínimo 10)	N_0 65-83% 1-3 38-54% > 3 13-26%
Tamaño tumoral	
Tipo histológico	
Grado nuclear (Bloom-Richardson)	Formaciones tubulares: > 75%; 10-75%; < 10% Pleomorfismo nuclear: Leve; media; máxima Núm. de mitosis: 0 a 5; 6 a 10; más de 11 GRADO: I: 3-5 II: 6-7 III: 8-9
Índices proliferativos	Índice mitótico, Timidina, Fase-S, Ki67, ciclinas

CARCINOMA DE MAMA

PRONÓSTICO

Factores analíticos y biomarcadores

ADN Celular: Aneuploides peor pronóstico.

Capacidad invasiva: La Catepsina D lo empeora.

Angiogénesis: Lo empeora

RFCE: HER-2/neu (c-ERB-B2) ⟷ Trastuzumab (Herceptin) Lapatinib

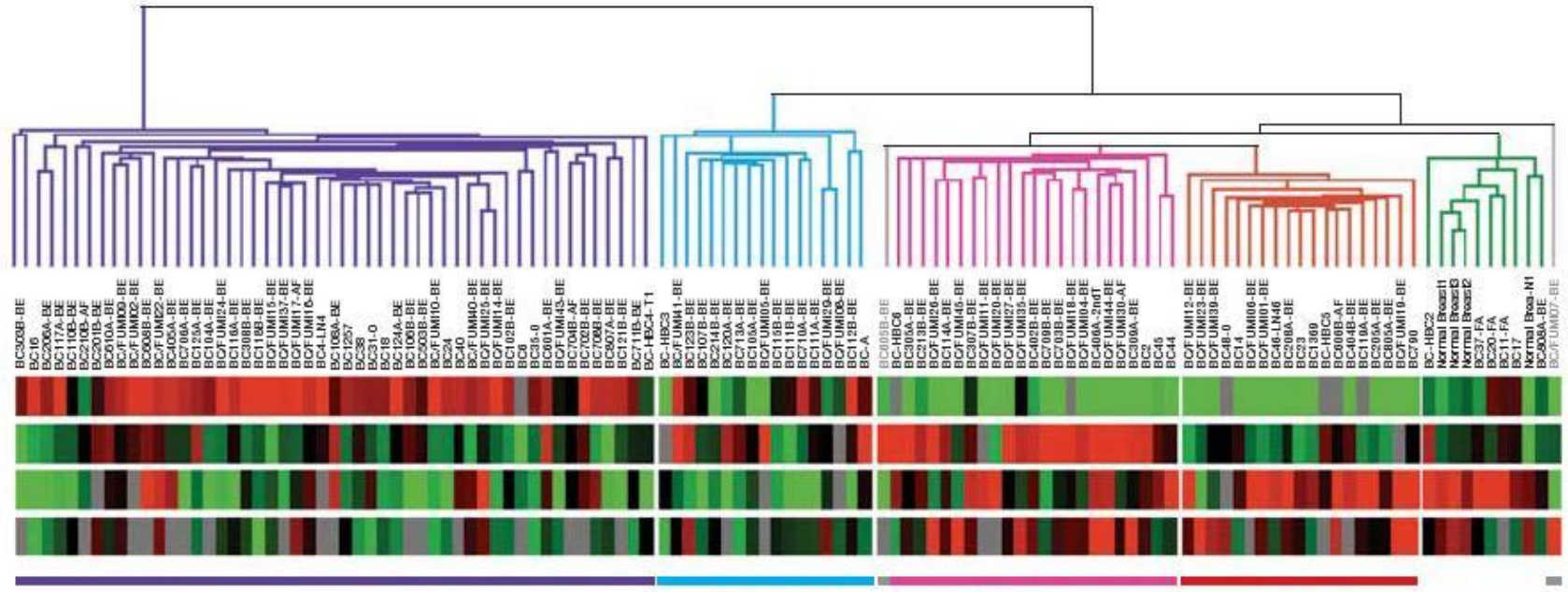
Topoisomerasa II alfa ⟷ Antraciclinas

Receptores hormonales (RH): RE; RPg lo mejoran

Proteínas reguladoras del ciclo celular: p53 lo empeora
bcl-2 lo mejora

Micro arrays

Figure 1. Immunohistochemical Identification of Breast Tumor Intrinsic Subtypes



Microarray-Based Breast Cancer Subtype[15, 17]	Luminal A	Luminal B	HER2+/ER-	Basal-like
				Normal Breast–like
Immunohistochemical Profile	ER+ and/or PR+, HER2-	ER+ and/or PR+, HER2+	ER-, PR-, HER2+	ER-, PR-, HER2-, CK5/6+ and/or HER1+

Gene Expression
(Fold Difference Relative to Median Level of Expression Across All Samples)

5.6 4 2.8 2 1.4 1 1.4 2 2.8 4 5.6

Lower — Median — Higher

Breast Cancer Subtypes and the Risk of Local and Regional Relapse

Table 1.

Summary of Immunohistochemical Criteria for Defining Breast Cancer Intrinsic Subtypes

Criteria and Subtype	ER	PR	HER2	CK5/6	EGFR	Ki-67
Criteria for positive result	> 1% of tumor nuclei	> 1% of tumor nuclei	HercepTest* 3+ or 2+ and FISH amplification ratio > 2.0	Any cytoplasmic or membranous staining	Any cytoplasmic or membranous staining	≥ 14% of tumor nuclei
Subtype						
Luminal A	Either ER or PR positive		Negative	Any	Any	Negative
Luminal B	Either ER or PR positive		Negative	Any	Any	Positive
Luminal-HER2	Either ER or PR positive		Positive	Any	Any	Any
HER2 enriched	Negative	Negative	Positive	Any	Any	Any
Basal-like	Negative	Negative	Negative	CK5/6 or EGFR positive		Any
TNP-nonbasal	Negative	Negative	Negative	Negative	Negative	Any

- Abbreviations: ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2; CK, cytokeratin; EGFR, epidermal growth factor receptor; FISH, fluorescent in situ hybridization; TNP, triple-negative phenotype.
- ⮠* Manufactured by Dako (Carpinteria, CA).

Breast Cancer Subtypes and the Risk of Local and Regional Relapse

Table 4.

Ten-Year LRFS After Breast-Conserving Surgery by Subtype

Subtype	No. of Patients	No. of Events	10-Year LRFS (%)	95% CI (%)
Luminal A	587	55	92	90 to 95
Luminal B	295	27	90	86 to 94
Luminal-HER2	61	5	91	83 to 100
HER2 enriched	80	15	79	69 to 89
Basal-like	134	19	86	80 to 93
TNP-nonbasal	114	9	92	86 to 97

- Abbreviations: LRFS, local relapse–free survival; HER2, human epidermal growth factor receptor 2; TNP, triple-negative phenotype.

Incidencia de metástasis por subtipo y localización

Kennecke et al

Table 2. Fifteen-Year Site-Specific Metastasis Cumulative Incidence Rates by Breast Cancer Subtype

Subtype	No. of Patients	Brain		Liver		Lung		Bone		Distant Nodal		Pleural/Peritoneal		Other	
		Incidence Rate (%)	95% CI (%)	Incidence Rate (%)	95% CI (%)	Incidence Rate (%)	95% CI (%)	Incidence Rate (%)	95% CI (%)	Incidence Rate (%)	95% CI (%)	Incidence Rate (%)	95% CI (%)	Incidence Rate (%)	95% CI (%)
Luminal A	1639	2.2	1.6 to 3	7.9	6.7 to 9.4	6.7	5.5 to 7.9	18.7	16.8 to 20.7	4.5	3.5 to 5.6	7.8	6.6 to 9.2	3.8	2.9 to 4.8
Luminal B	893	4.7	3.4 to 6.2	13.8	11.6 to 16.2	13.4	11.2 to 15.8	30.4	27.4 to 33.5	9.6	7.8 to 11.7	14.7	12.5 to 17.2	8.1	6.4 to 10
HER2 positive, ER/PR positive	244	7.9	4.8 to 12	21.3	16.3 to 26.7	17.7	13.2 to 22.8	30.9	25.2 to 36.7	10.5	7 to 14.8	16	11.7 to 21	6.6	3.9 to 10.2
HER2 positive, ER/PR negative	266	14.3	10.4 to 18.8	23.3	18.4 to 28.6	24.1	19.1 to 29.3	30.1	24.7 to 35.7	13	9.2 to 17.4	16.2	12 to 20.9	8.8	5.8 to 12.7
Basal-like	367	10.9	8 to 14.3	9.3	6.6 to 12.5	18.5	14.7 to 22.7	16.6	13 to 20.6	17.2	13.5 to 21.2	12.8	9.6 to 16.5	10.4	7.5 to 13.7
TN nonbasal	318	7.2	4.7 to 10.4	10.7	7.6 to 14.4	12.5	9.1 to 16.5	15.1	11.4 to 19.4	12.3	8.9 to 16.1	9.2	6.3 to 12.7	9.2	6.2 to 12.9
P		< .001		< .001		< .001		< .001		< .001		< .001		< .001	

NOTE. *P* values are based on Gray's test comparing cumulative incidence curves across subtypes.
Abbreviations: HER2, human epidermal growth factor receptor 2; ER, estrogen receptor; PR, progesterone receptor; TN, triple negative.

CARCINOMA DE MAMA

TÉCNICAS DIAGNÓSTICAS

Tumor palpable
Imagen Rx en revisión o screening

Mamografía
RNM
PET

Muestra para A. Patológica
- PAAF
- Aguja gruesa
- Biopsia incisional / excisional
- Localización con arpón
- Biopsia esterotáxica aguja gruesa
- ROLL

BIRADS

American College of Radiology
Breast Imaging Reporting And Data System

- 0: Necesita evaluación adicional por imagen
- 1: Negativo
- 2: Hallazgo benigno
- 3: Probablemente benigno. Seguimiento a 6 meses.
- 4: Anormalidad sospechosa. Considerar biopsia.
- 5: 95% de probabilidad de ser maligna.
- 6: Malignidad probada mediante biopsia.

CARCINOMA DE MAMA

TRATAMIENTO QUIRÚRGICO

3000 A de C

Enfermedad local (Halsted 1852-1922)

Enfermedad general

Cirugía cada vez menos agresiva

Cirugía conservadora + RT = Cirugía radical (NSABP B-06 años 80)

CARCINOMA DE MAMA

TÉCNICAS QUIRÚRGICAS

Tumorectomía
Segmentectomía
Cuadrantectomía
Mastectomía simple
Mastectomía subcutánea
Mastectomía radical — Halsted, Patey, Madden

Linfadenectomía axilar — 2 / 3 niveles de Berg
Ganglio centinela

CARCINOMA DE MAMA

CIRUGÍA CONSERVADORA

Indicadas

- T < 4-5 cm
- Estadios III que responden a QT preoperatoria
- Si se supone buen resultado estético
- Ausencia de contraindicaciones para RT
- Información y consentimiento
- CDIS no comedo
- E. Paget sin tumor asociado

Dudosas

- T > 5 cm
- CDIS extenso asociado
- CDIS tipo comedo
- Dificultad de seguimiento

CARCINOMA DE MAMA

CIRUGÍA CONSERVADORA

Contraindicadas

Lesión grande para tamaño de la mama
Si se supone mal resultado estético
Multicéntricos
N2
Margen afectado
Conectivopatías
Gestación
Rechazo de la paciente

CARCINOMA DE MAMA

COMPLICACIONES CIRUGÍA

Intraoperatorias	Vasculares Neumotórax Lesión nerviosa
Precoces	Hemorragia Seroma Infección Lesiones cutáneas Parestesias
Tardías	Linfedema Cicatrización patológica

CARCINOMA DE MAMA

TRATAMIENTO NEOADYUVANTE

Se administra antes de la cirugía para reducir su extensión. Para tumores localmente avanzados y estadios II y III A que irían a mastectomía por tamaño desfavorable.

Evalúa la respuesta al tratamiento
La QT frena la progresión tumoral en 97%
Mejora el índice de CC
Disminuye incidencia de N+ axilares

CARCINOMA DE MAMA

TRATAMIENTO ADYUVANTE

Se administra después de la cirugía para atacar las micrometástasis.
Años 70 Milan (CMF); NSABP (Melphalan)

QUIMIOTERAPIA

La QT mejora la supervivencia
Poli mejor que mono
La de 6 meses = 12 meses
Beneficia a Pre y Post; No y N+
Mejor QT con HT que sola
No sirve en Axila – y T< 1cm
T 1-2cm, Grado I, Axila –
> 70 años

CMF X 6
AC X 4
Taxanos + Antraciclinas en N+

CARCINOMA DE MAMA
TRATAMIENTO ADYUVANTE

TOXICIDAD DE LA QUIMIOTERAPIA

AGUDA — Neutropenia y sepsis

Alopecia, náuseas, vómitos, astenia

CRÓNICA — Pérdida de función ovárica
Miocardiopatía por Antraciclinas
Leucemias y S. mielodisplásicos

CARCINOMA DE MAMA

TRATAMIENTO ADYUVANTE

HORMONOTERAPIA

El Tamoxifeno (TAM) se une a los RE
Beneficia a Pre y Post; N0 y N+
Debe durar > 3 años

Inhibidores de aromatasa en M1 mejor que TAM

CARCINOMA DE MAMA

TRATAMIENTO ADYUVANTE

TOXICIDAD DE LA HORMONOTERAPIA

Síntomas menopáusicos
Tromboembolismos
Ca de Endometrio (TAM)

CARCINOMA DE MAMA

TRATAMIENTO ADYUVANTE

RADIOTERAPIA

TRAS MASTECTOMÍA
- T grandes
- 4 ó más N
- Extensión extracapsular

TRAS CC
- Previene recidivas
- En Estadios I y II

RT Externa
Sobreimpresión (Boost)

CARCINOMA DE MAMA

TRATAMIENTO ADYUVANTE

TOXICIDAD DE LA RADIOTERAPIA

Piel: eritema, descamación
Neumonitis
Cardíaca
Plexo braquial
Linfedema braquial
Tumores radioinducidos

CARCINOMA DE MAMA

CARCINOMA LOCALMENTE AVANZADO

T3 > 5 cm
T4 a, b y c
N2
M1 supraclaviculares
Ca inflamatorio

TRATAMIENTO

QT Neoadyuvante: Taxanos, antraciclinas, vinorrelbina
Cirugía: MR + LA
QT + HT
RT

CARCINOMA DE MAMA

CARCINOMA INFLAMATORIO DE MAMA

Edema de piel
Eritema
Calor
No tumor
Adenopatías

Ca ductal infiltrante
Poco diferenciado
RH –
Signos de mal pronóstico:
c-erb-2; p53

Dx diferencial con mastitis
Emboliza linfáticos dérmicos

QT ⟶ MR+ LA ⟶ QT + RT

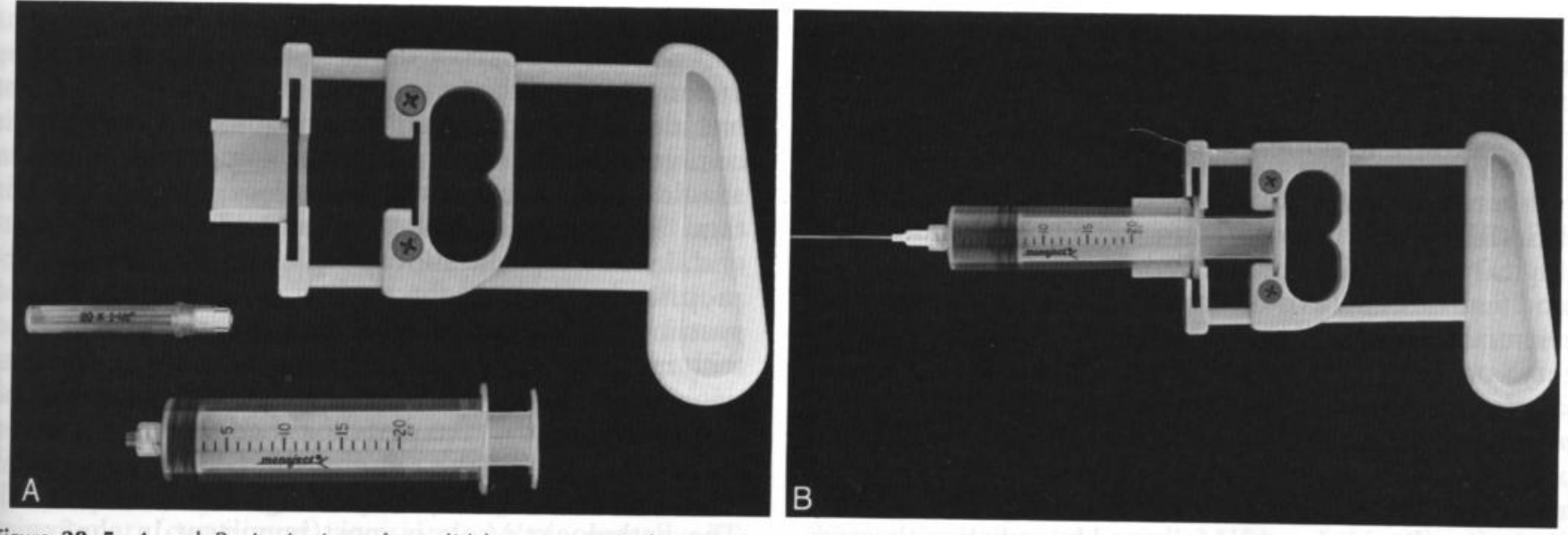


Figure 28–5. *A* and *B*, Aspiration of a solid breast mass is best performed using a cytology fine needle "aspiration gun" (Cameco, Enebyberg, Sweden).

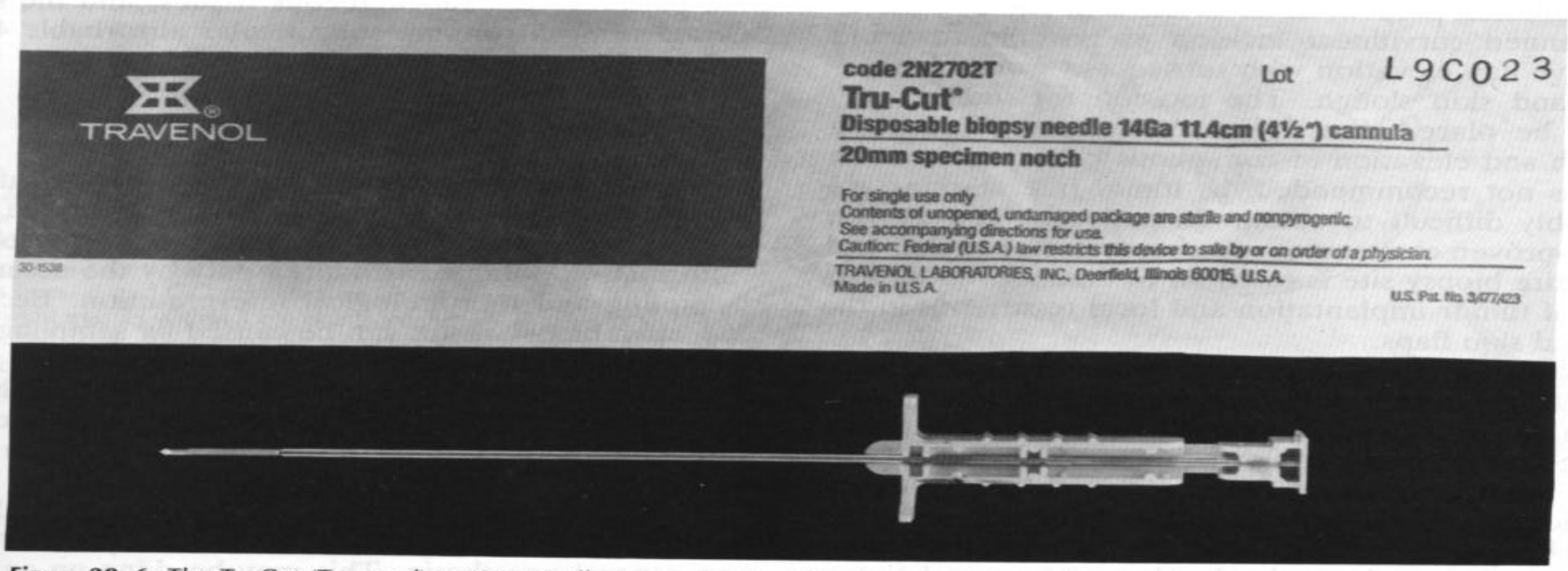
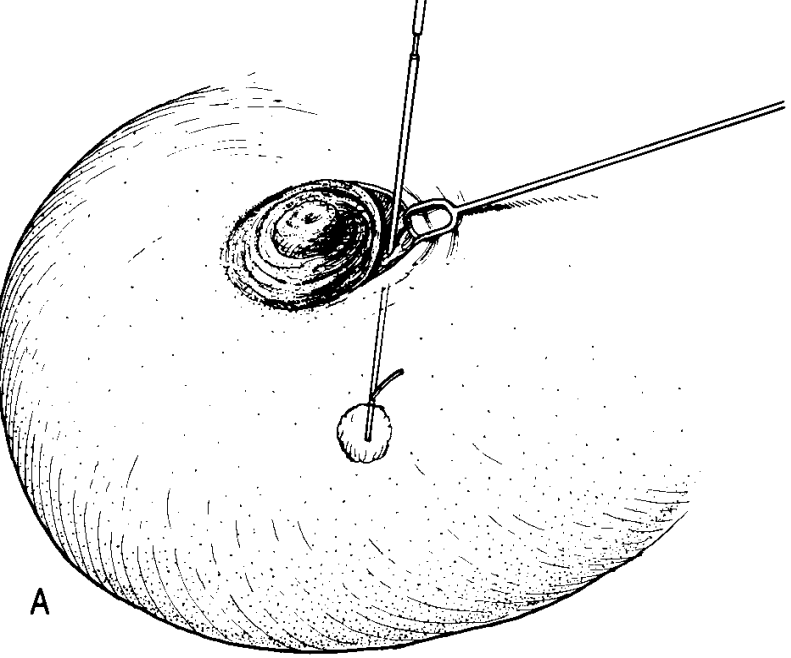


Figure 28–6. The TruCut (Travenol) cutting needle is commonly utilized to obtain a core biopsy of solid, palpable breast masses.



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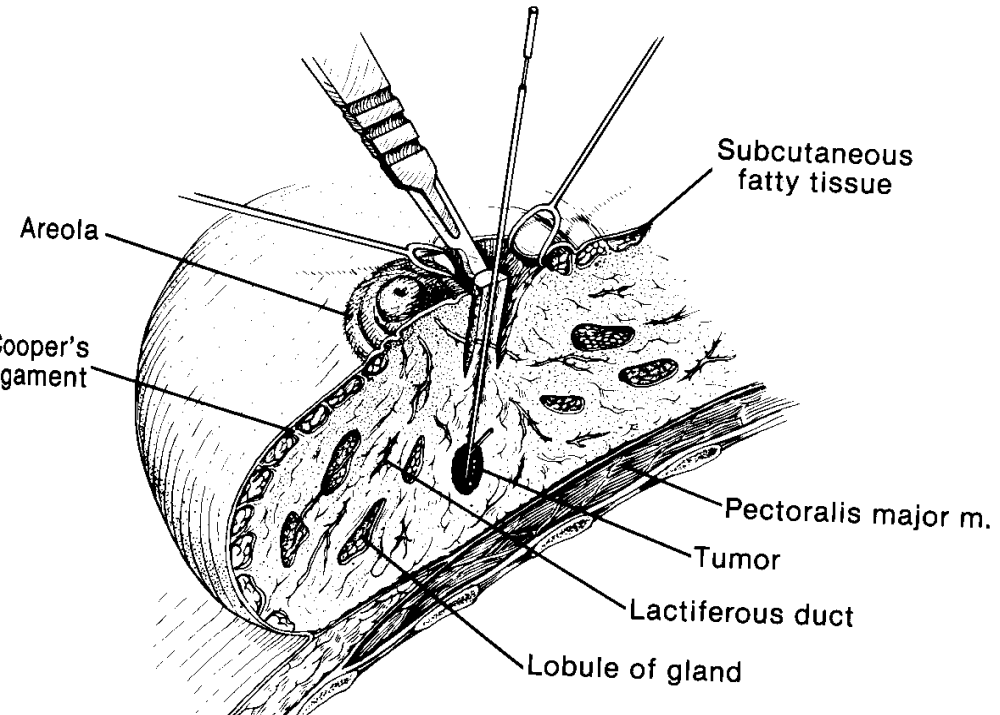
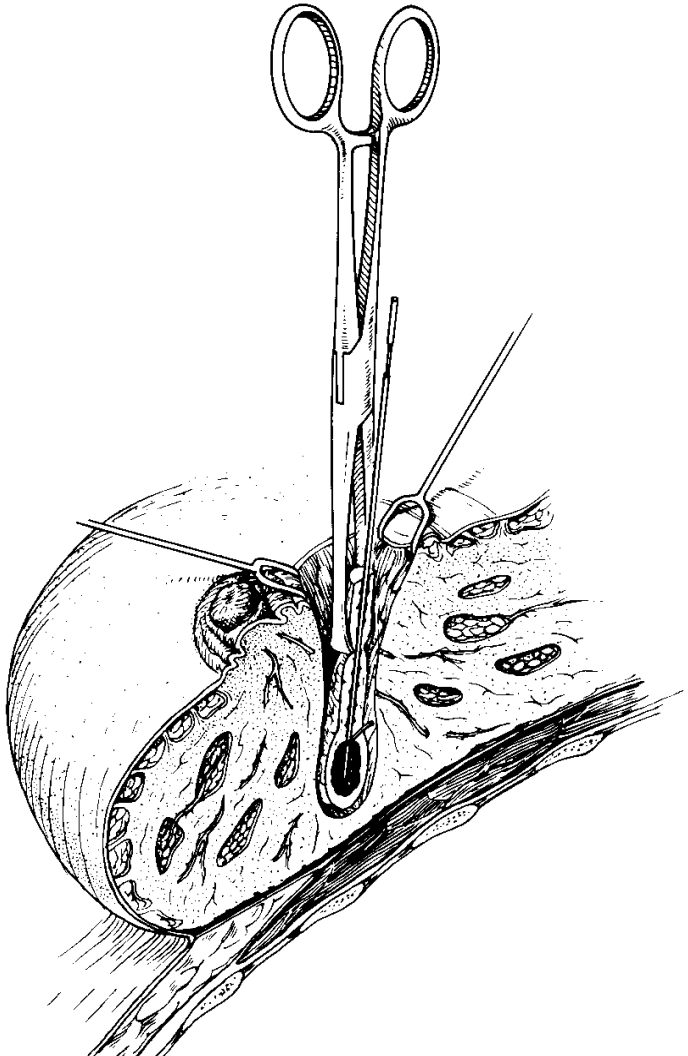
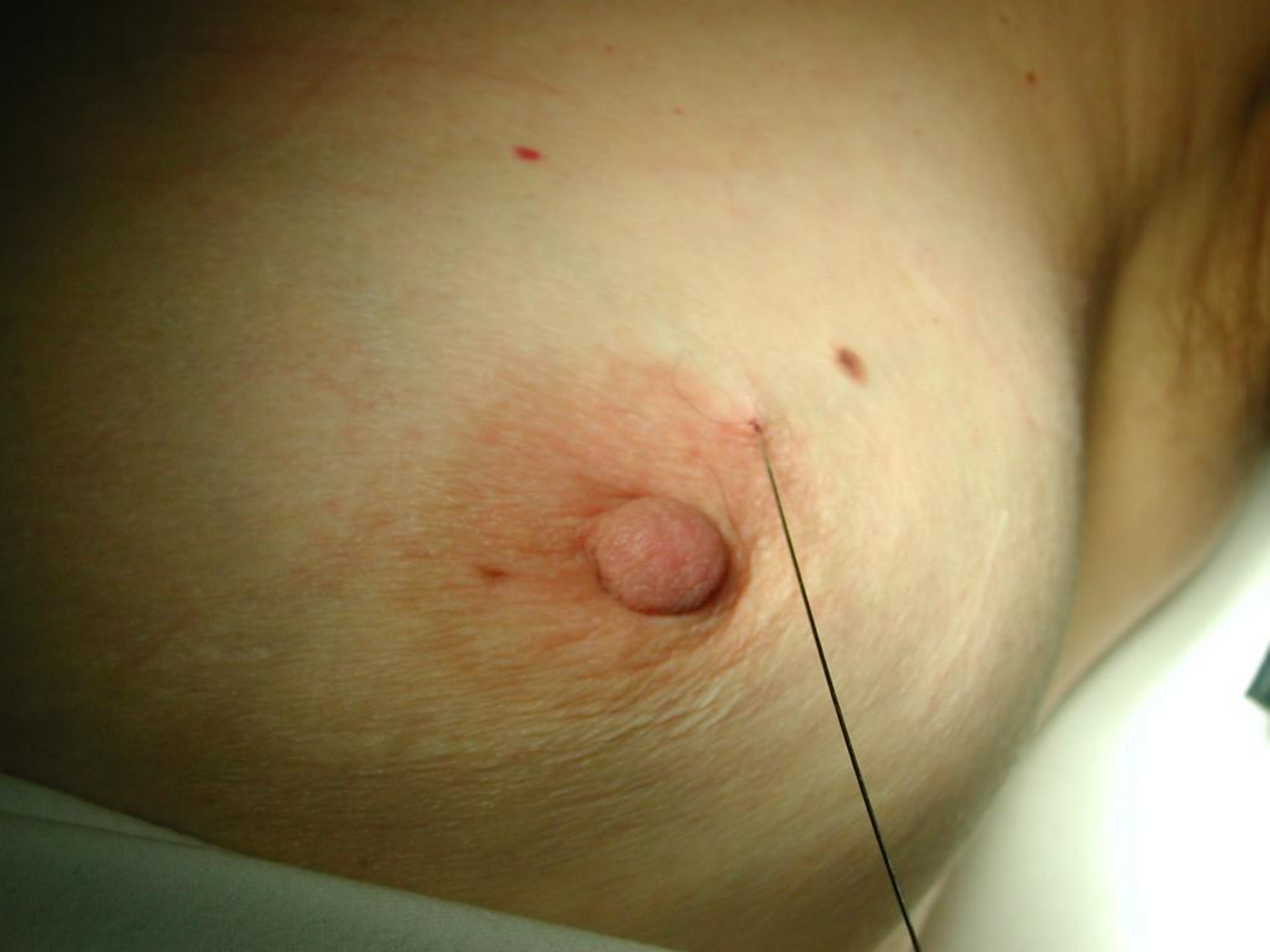
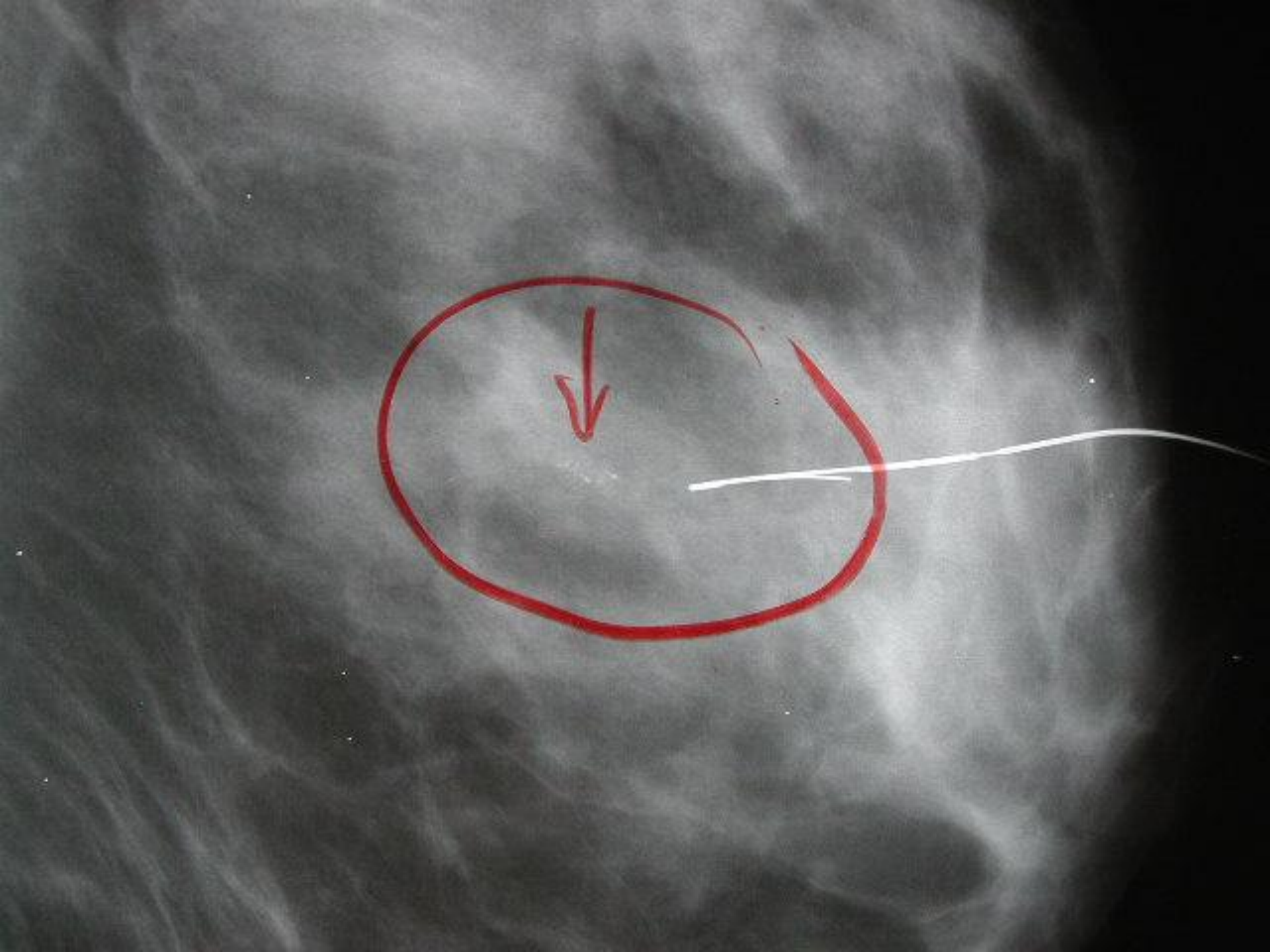
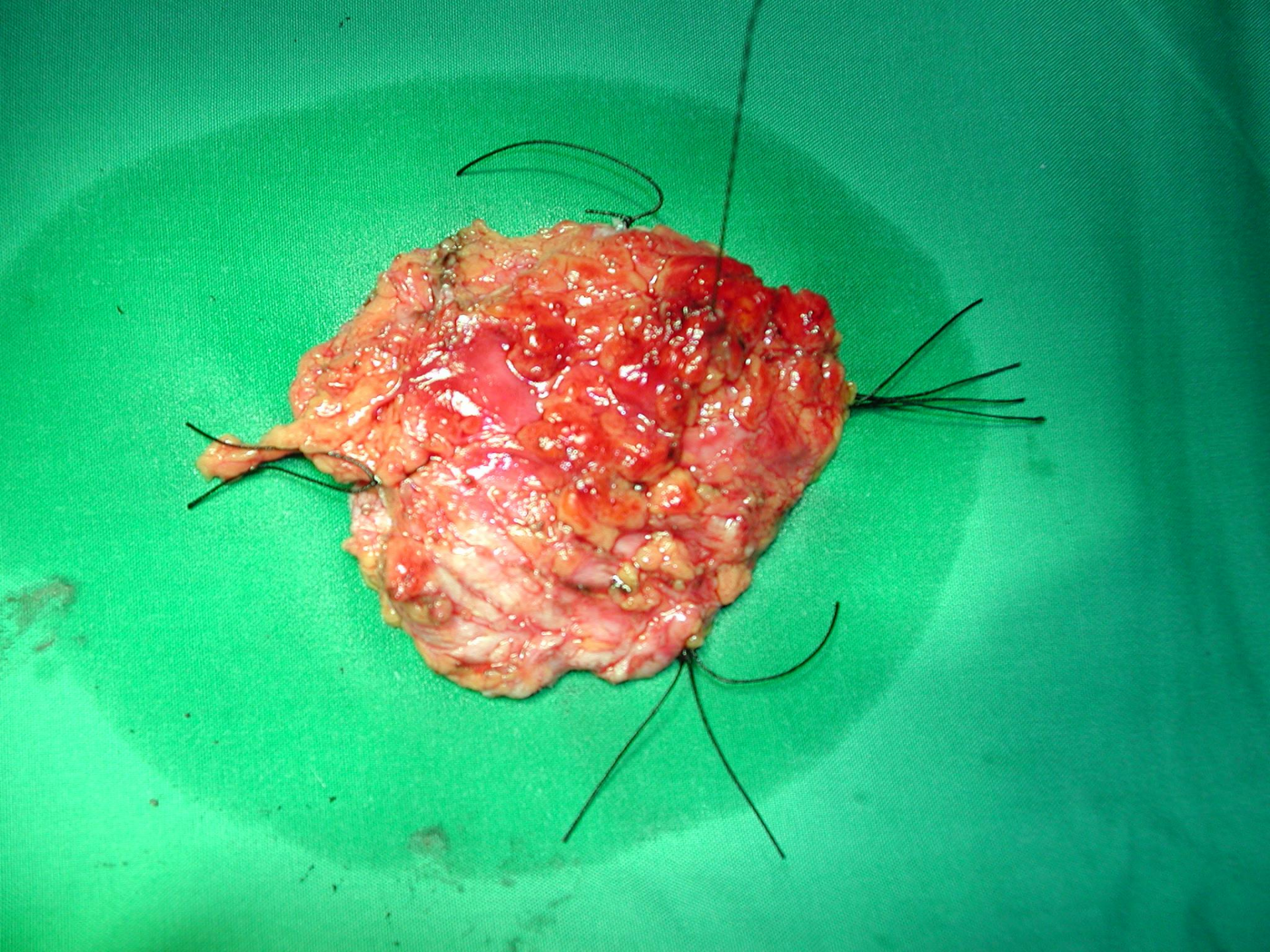
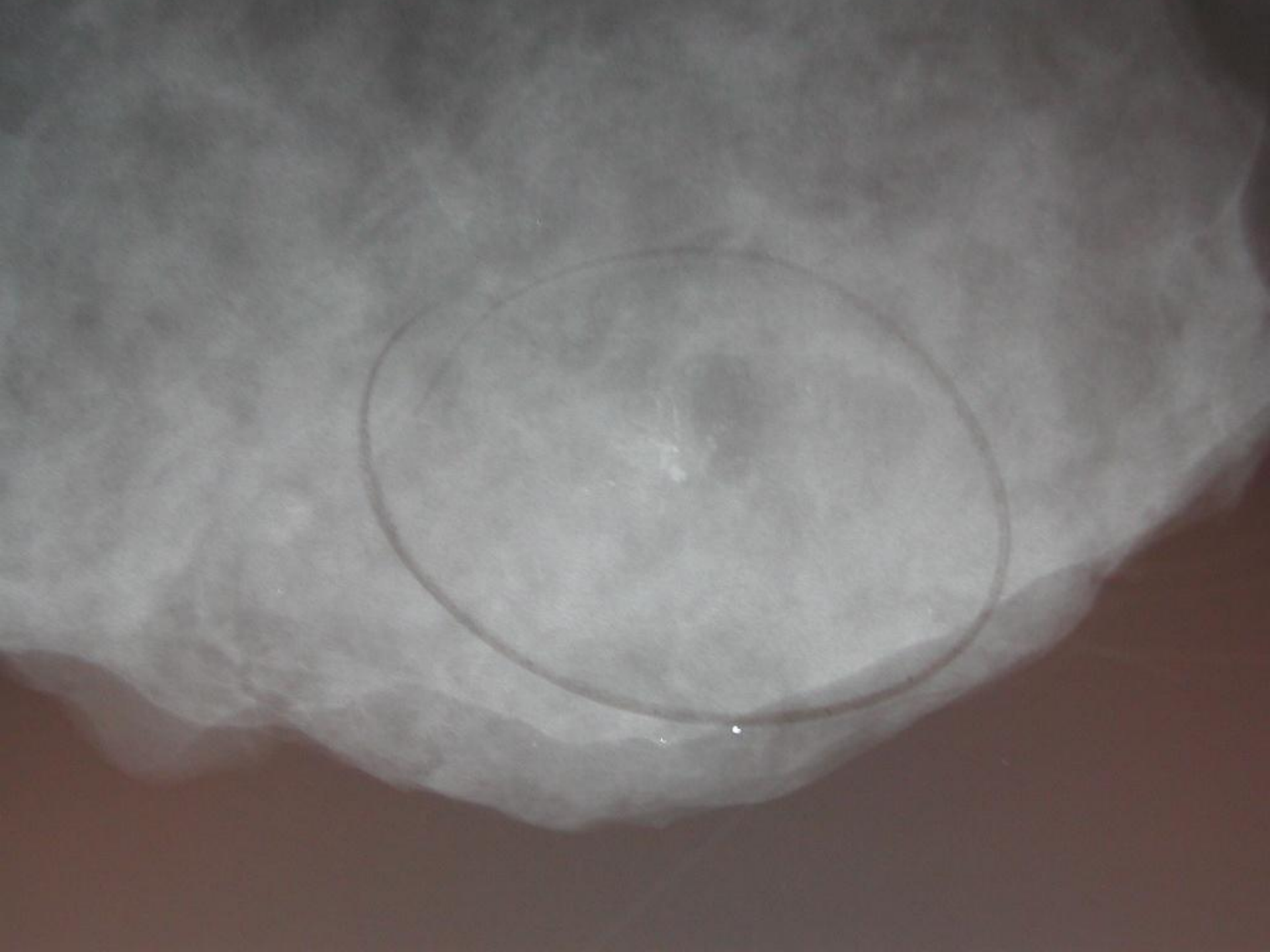

Subcutaneous fatty tissue
Areola
Cooper's ligament
Pectoralis major m.
Tumor
Lactiferous duct
Lobule of gland

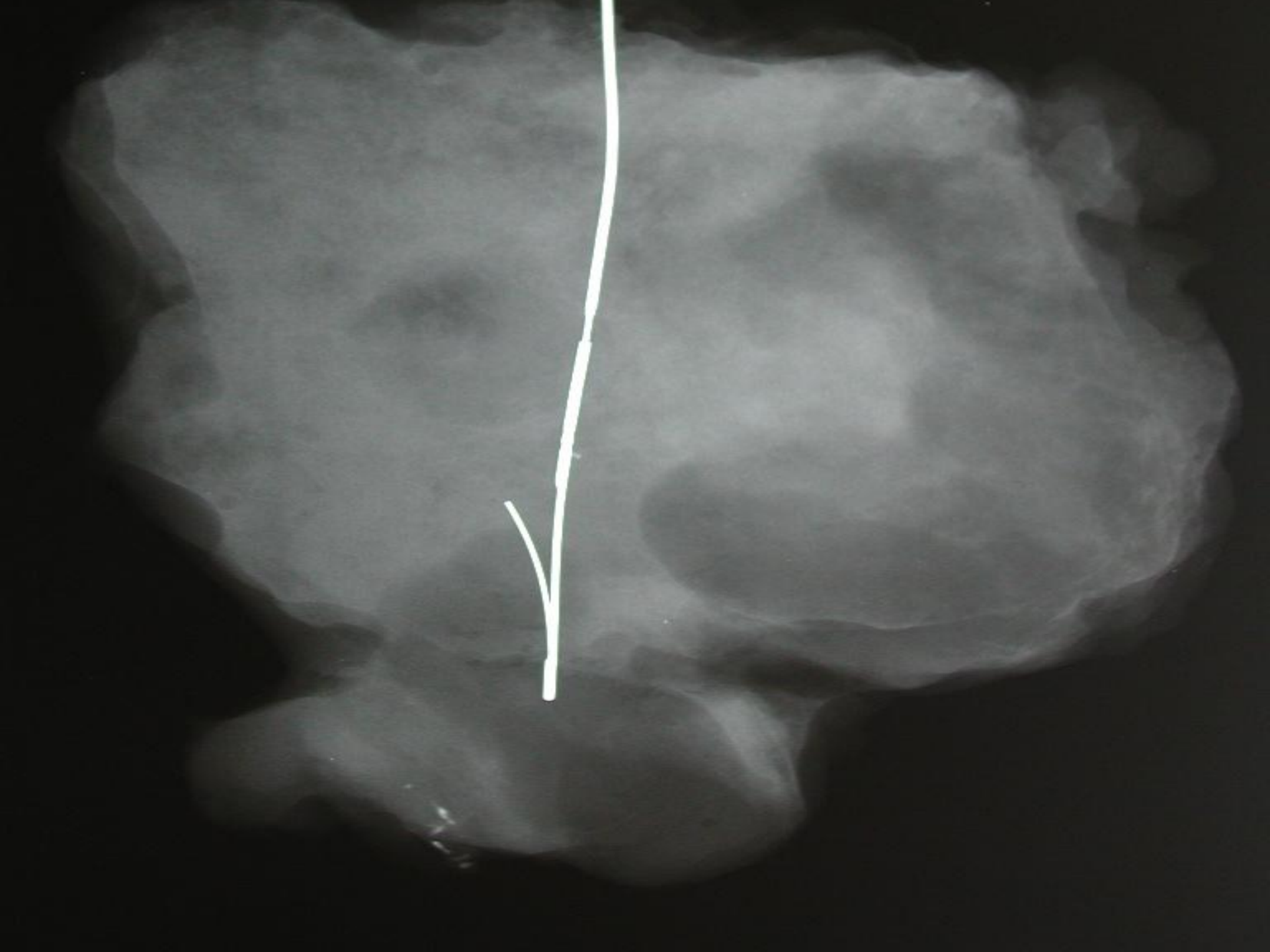


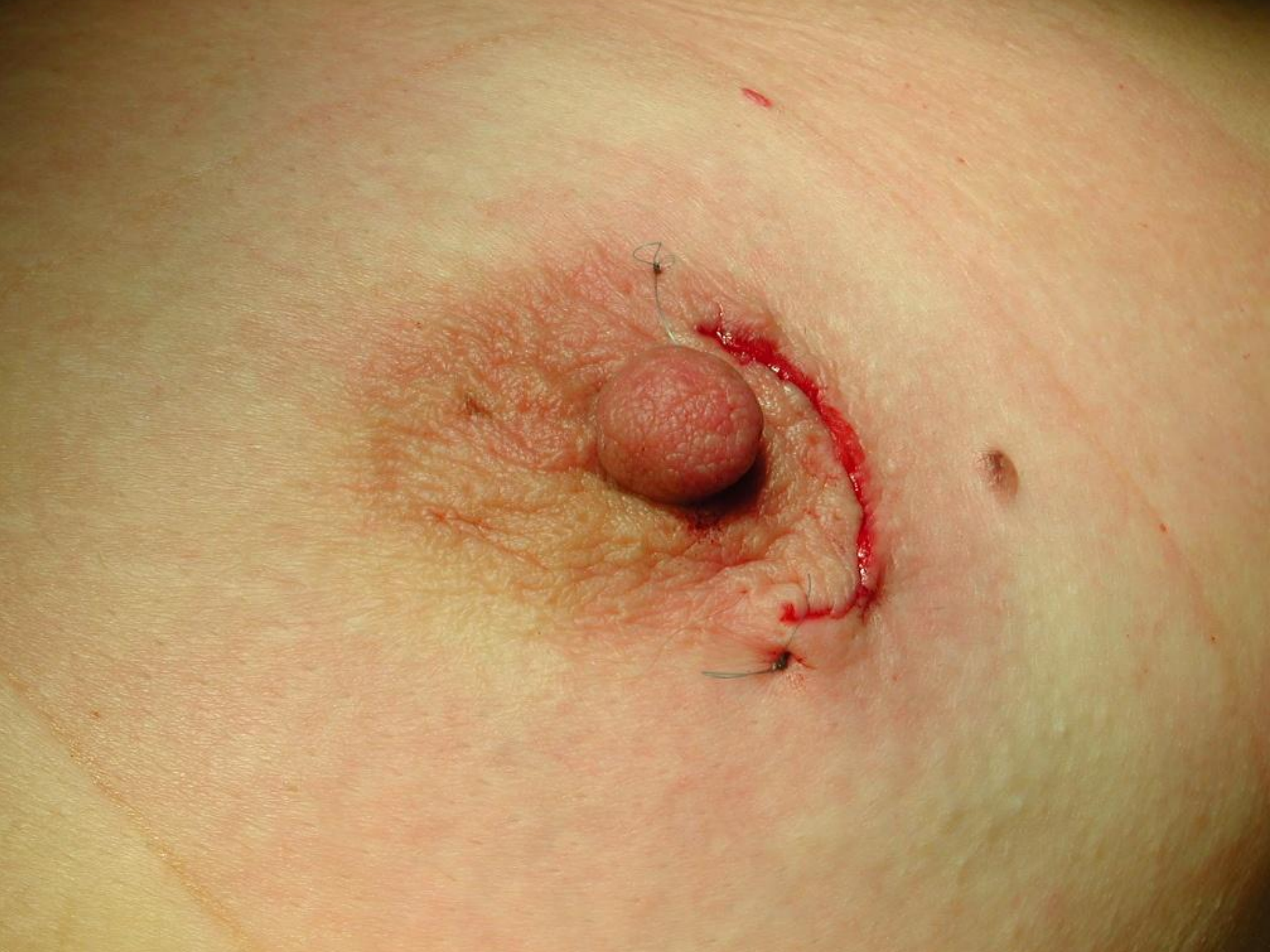












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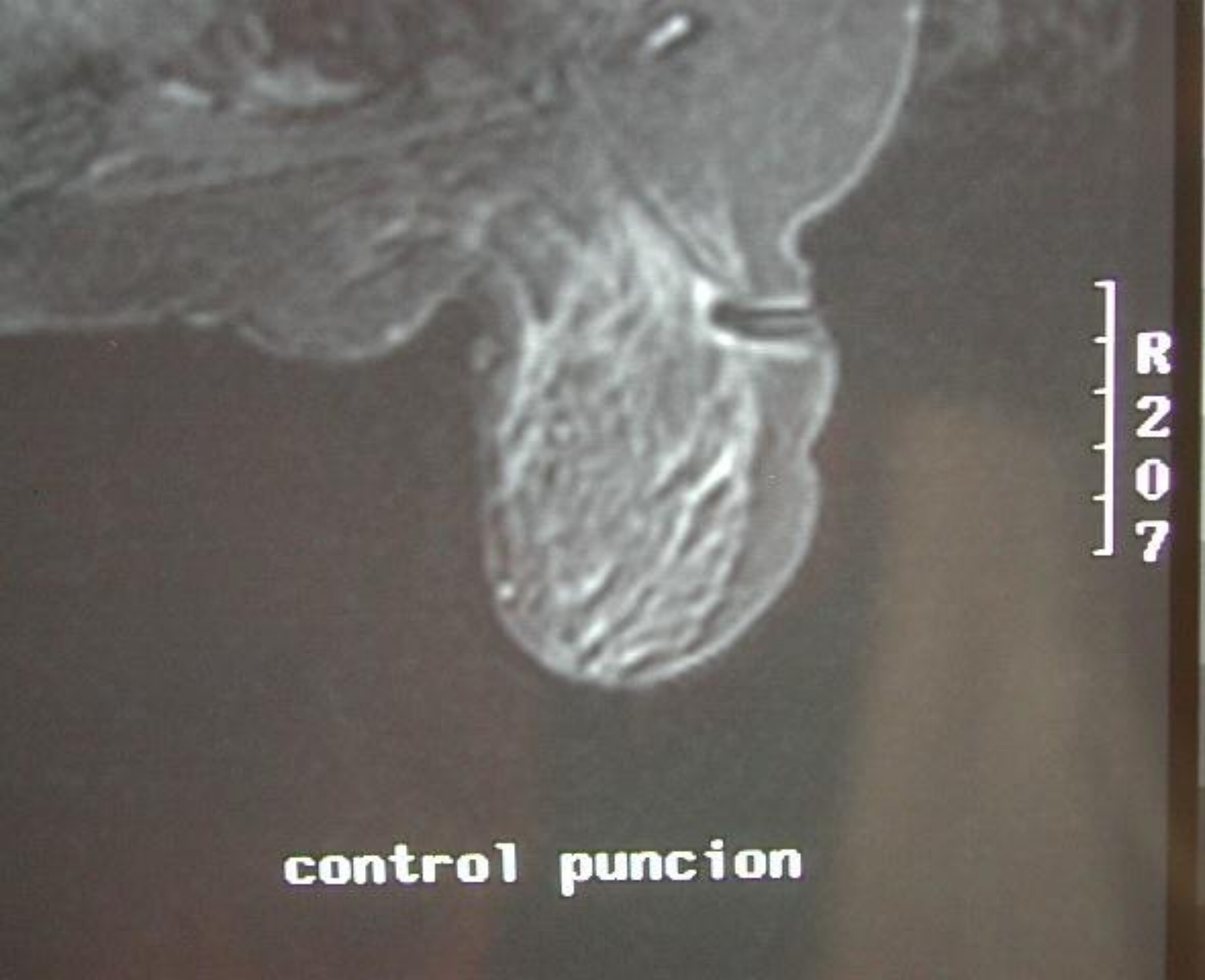
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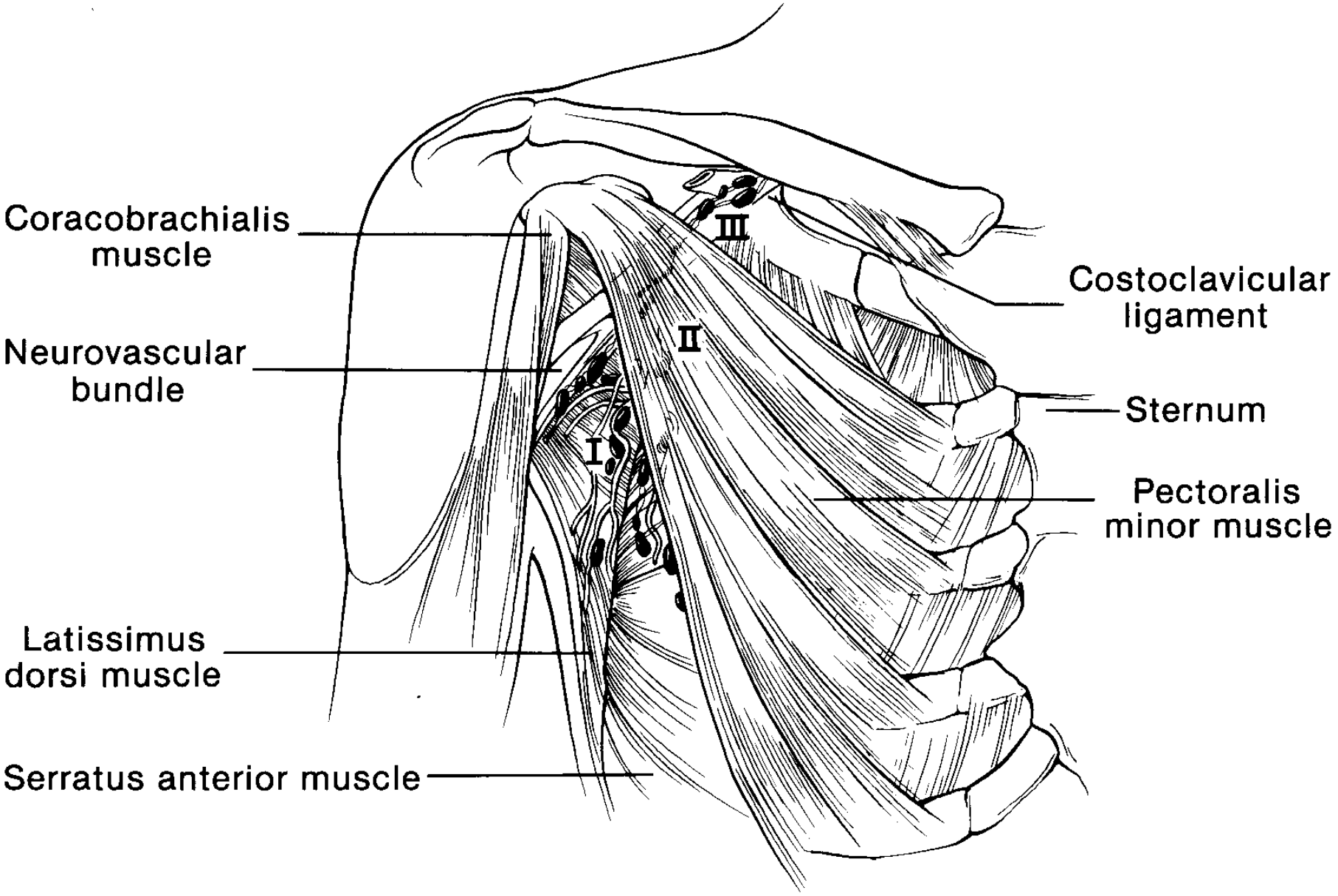
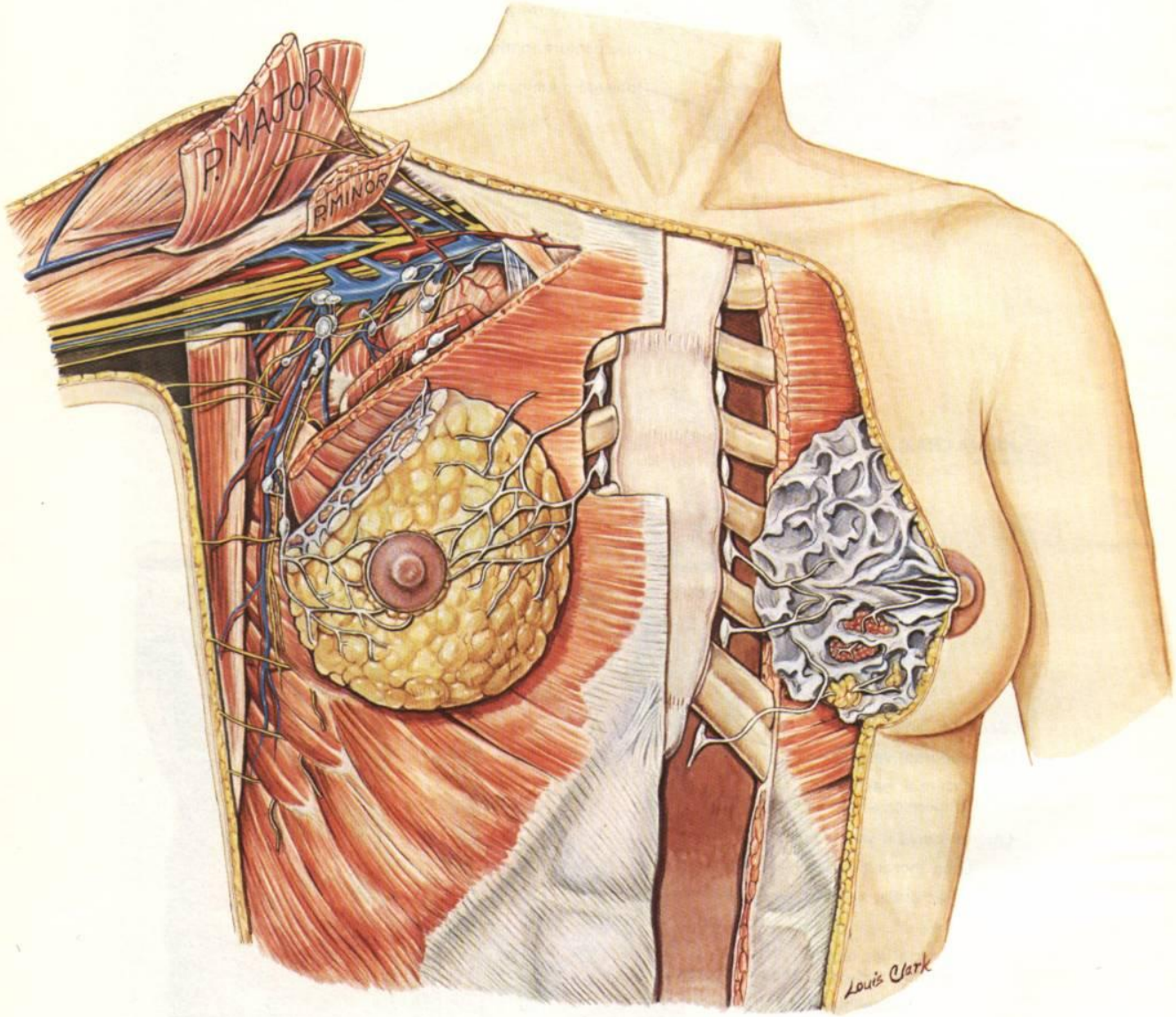

Coracobrachialis muscle
Neurovascular bundle
Latissimus dorsi muscle
Serratus anterior muscle
III
II
I
Costoclavicular ligament
Sternum
Pectoralis minor muscle


P. MAJOR
P. MINOR
Louis Clark