Terapia Hormonal de reemplazo, su impacto en los métodos de diagnóstico

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THR y su impacto en las imágenes

- Screening con mamografía
- THR y densidad mamaria
- Mama densa
- THR y screening con mamografía
- THR e IRM

Mamografía

- Mamografía es el principal método de imágenes, probado por la evidencia médica para la detección temprana de lesiones neoplásicas en la mama

- Es el “único” método de screening recomendado por los grupos de consenso excepto en pacientes definidas como de “alto riesgo”

Mamografía

- Mamografía diagnóstica es aquella que realizamos en pacientes que son derivadas por síntomas o signos clínicos y en las que generalmente realizamos mas de un examen diagnóstico

- Mamografía de "cribado", "screening", "control anual" es la mamografía que realizamos en pacientes asintomáticas, que vienen anualmente a control sin síntomas o signos clínicos

Mamografía - Screening

- Se recomienda una mamografía de base a los 35 años para evaluar el tipo de parénquima glandular
- Una mamografía anual, a partir de los 40 años
- En algunos casos es tolerable realizar una mamografía cada 2 años, según tipo de mama, AF, factores de riesgo, etc.

Mamografía

- No existe ninguna prueba o grupo de pruebas que pueda asegurar que una mujer “no” tiene cáncer de mama
- Los estudios de screening “no” son perfectos
- Principal limitación son las mamas densas
- Una mamografía normal en una paciente con hallazgos clínicos sospechosos no descarta la existencia de un cáncer de mama

Screening – Algunos Datos

- ⇩ de la mortalidad por cáncer de mamas → 20-35%

- Sobrevida a los 20 años

87.3% ⇨ tumores ≤ 0.9cm

83.8% ⇨ tumores 1-1.4cm

Mamografía

Sensibilidad de la mamografía de screening varia con:

- Edad
- Densidad
- AF

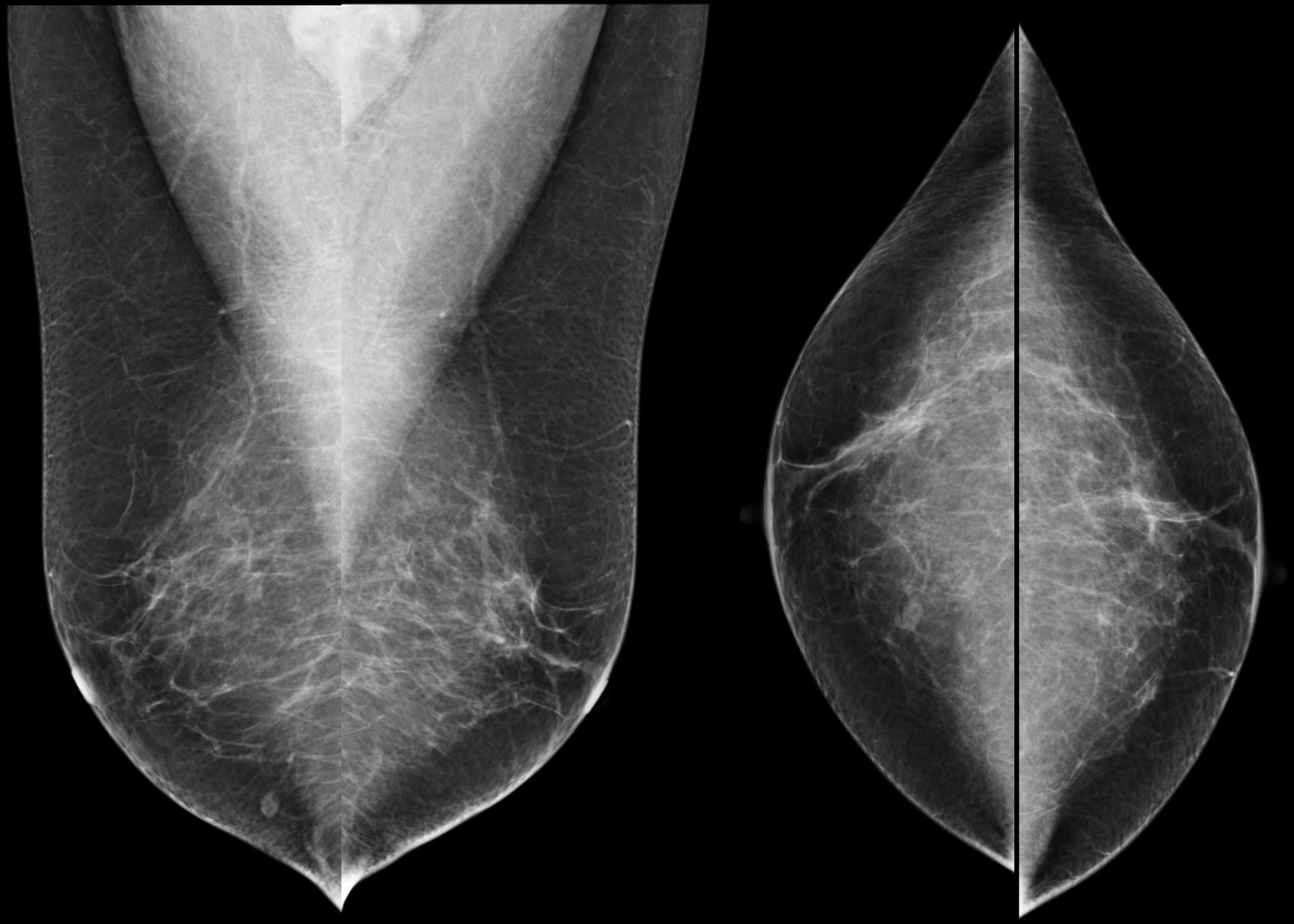
→ Porcentaje de tejido fibroglandular vs tejido lipomatoso

Mamografía – ACR

Hay 4 patrones glandulares:

- Involución lipomatosa ➡ tipo a
- Involución lipomatosa con densidades en parches ➡ tipo b

- Tejido glandular heterogéneamente denso de distribución homogénea ➡ tipo c
- Tejido glandular extremadamente denso y homogéneo ➡ tipo d



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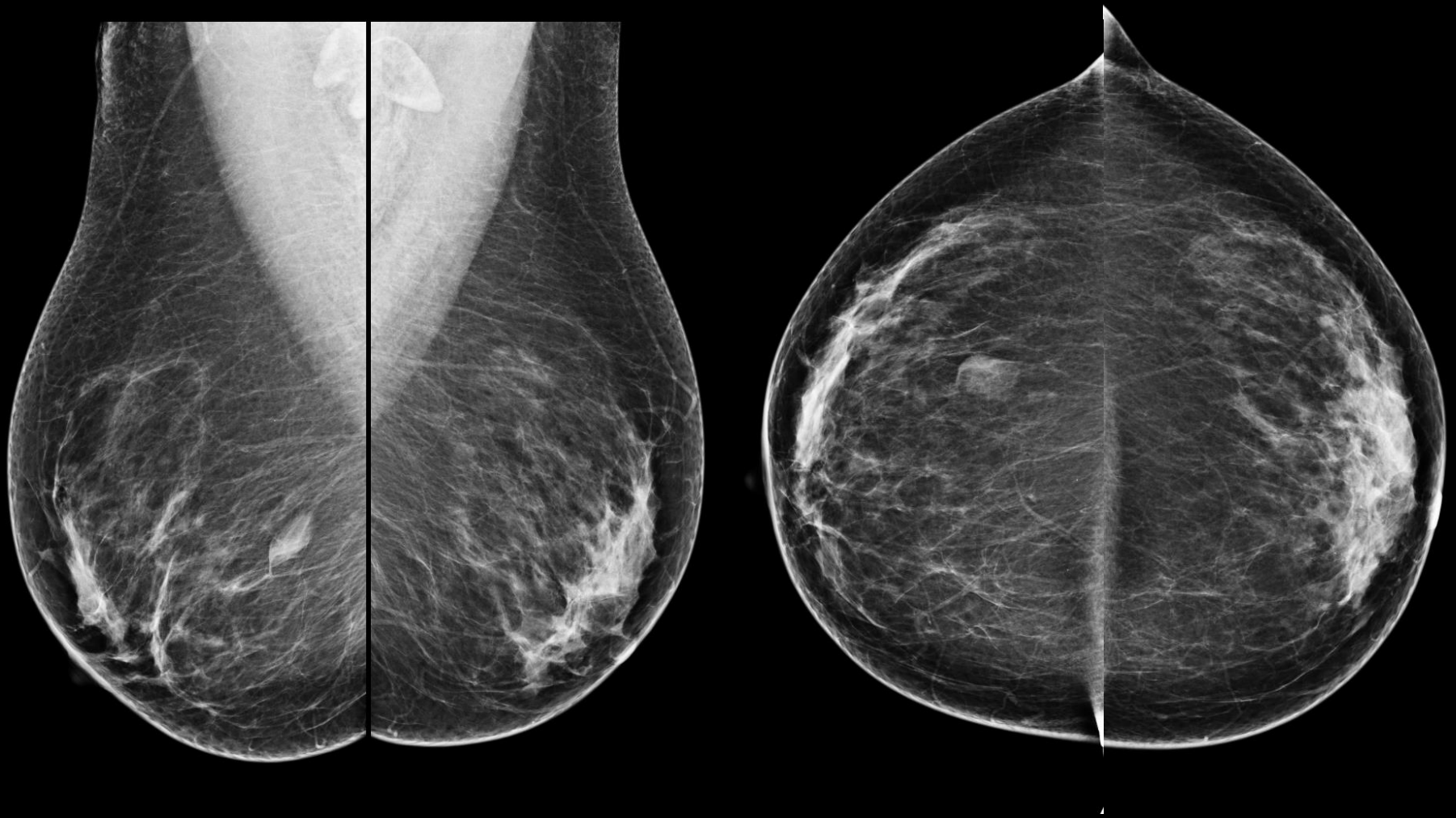
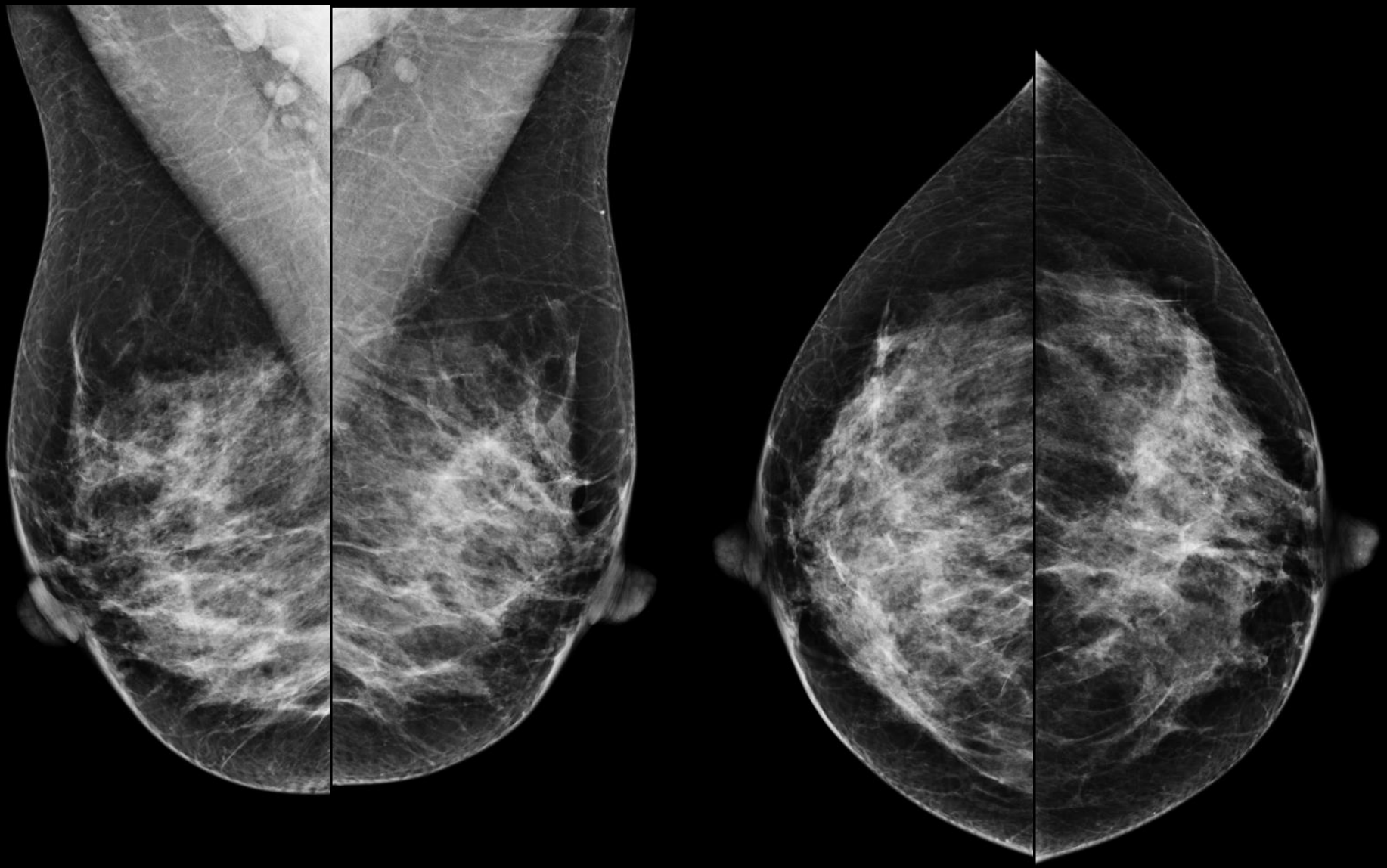
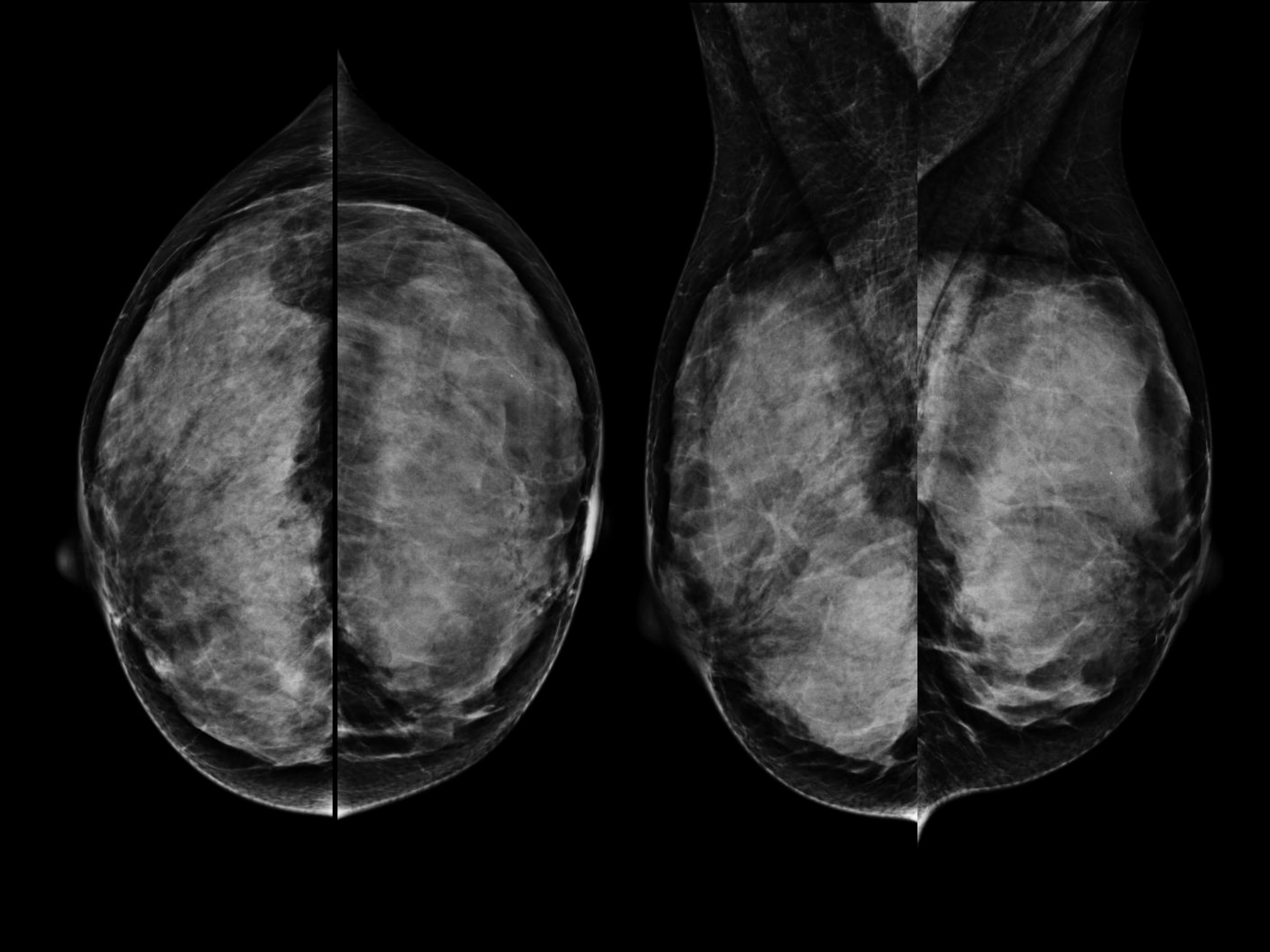




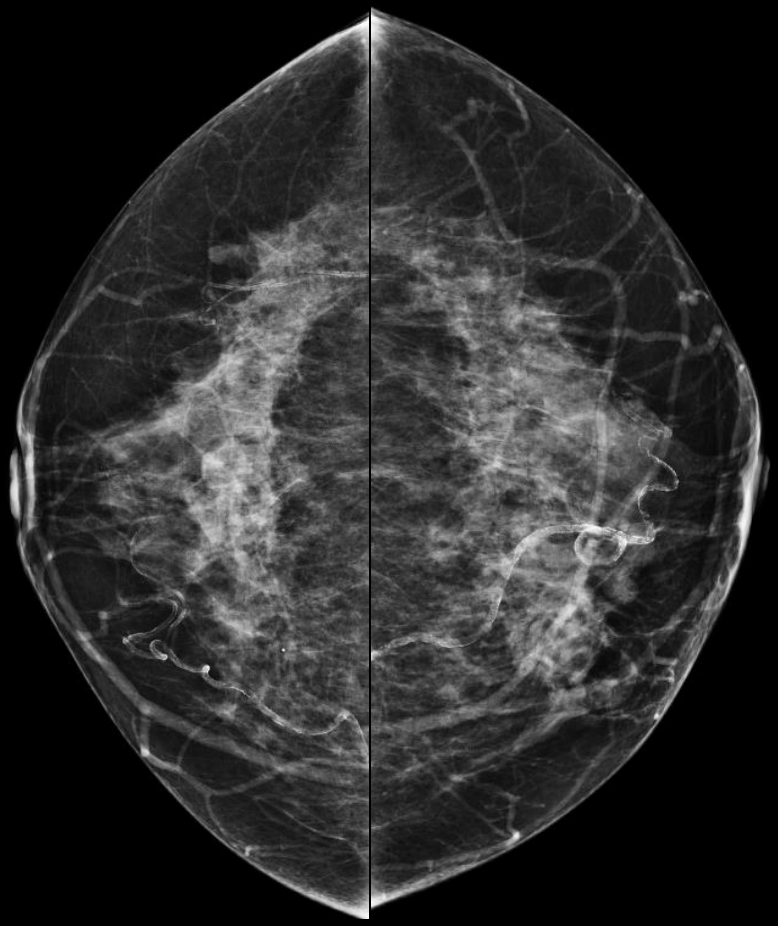


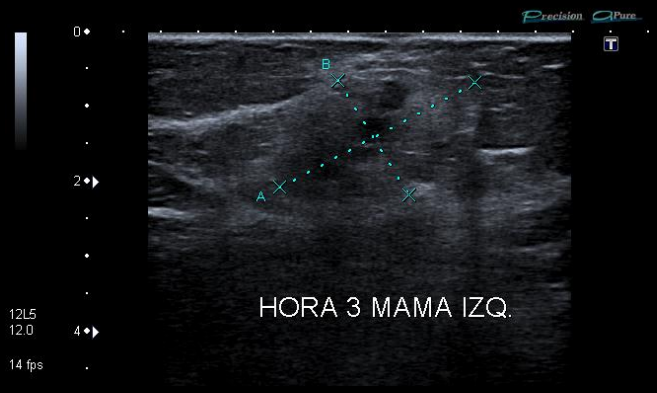
Mama densa

Las pacientes con mama densa tienen 3-5 veces más riesgo de padecer un cáncer que las pacientes con mamas lipomatosas.

Wolfe et al
Cancer 1976

Pacientes que se benefician con US de screening
Ecografía volumétrica automatizada

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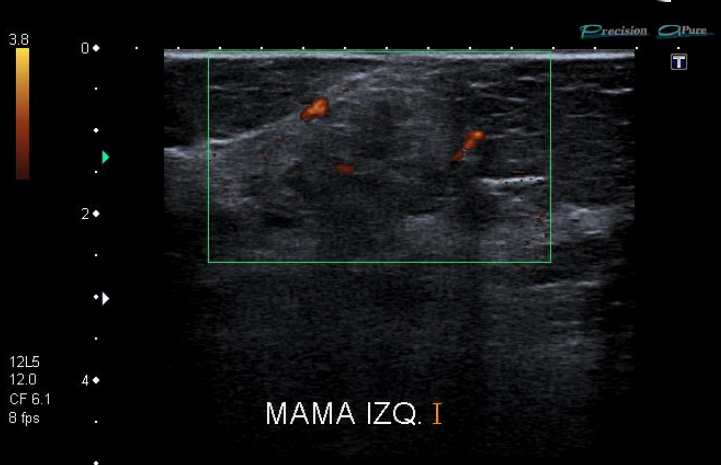
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¿De qué depende la densidad mamaria?

- Tejido fibroso-sostén
- % de tejido lipomatoso
- Cantidad de tejido epitelial

Factores que modifican la densidad de la mama

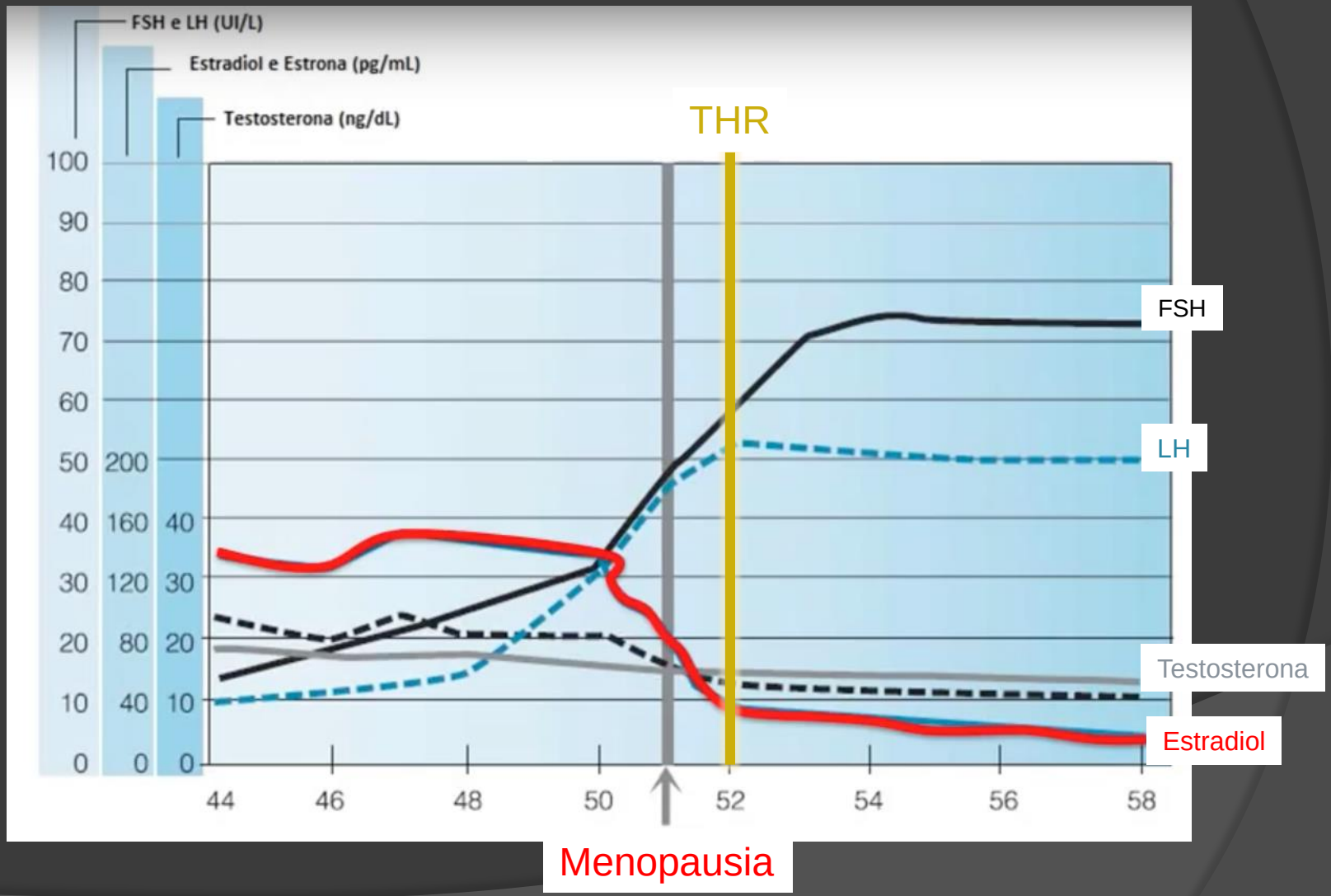
Aumentan la densidad

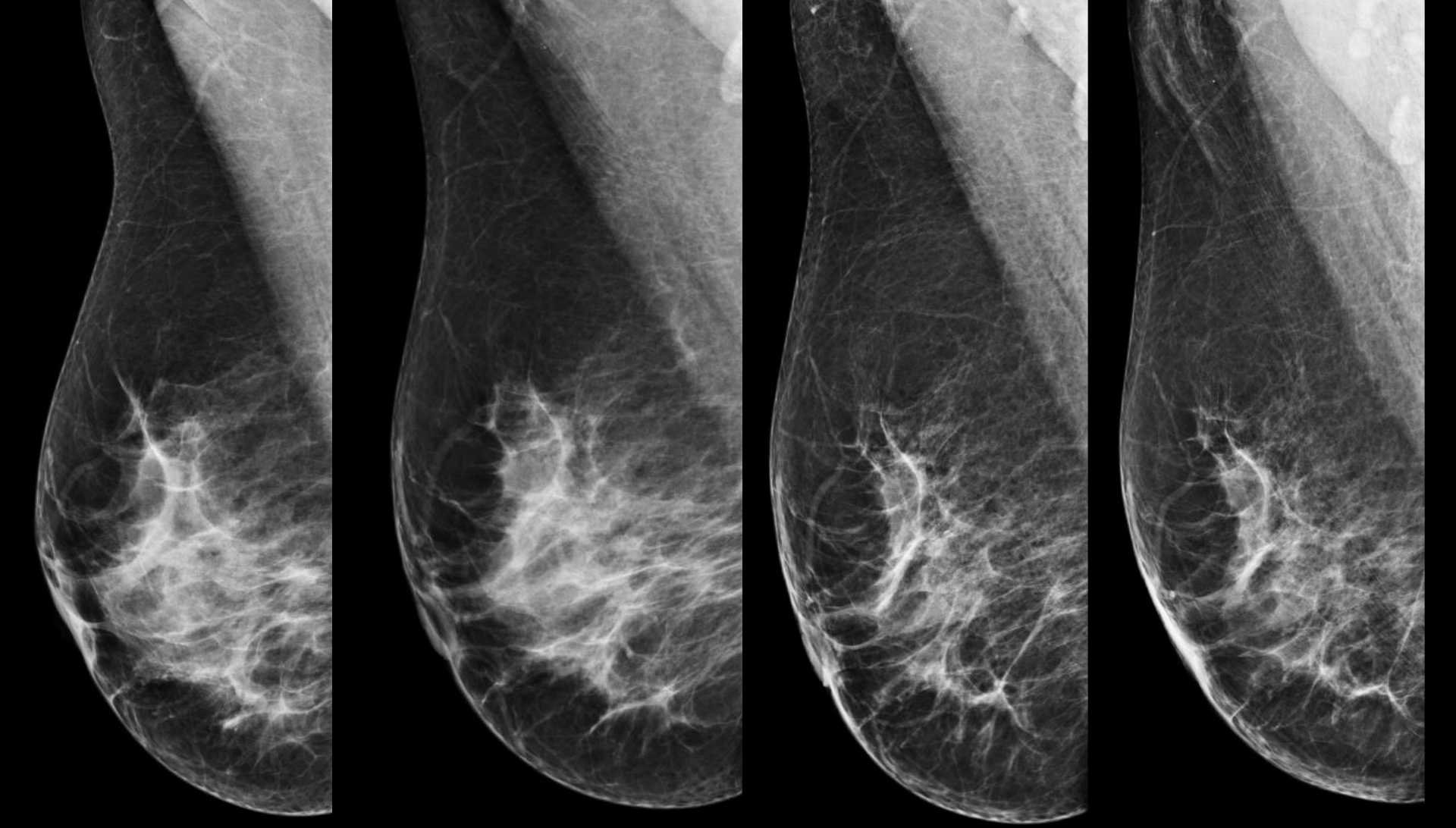
- Pérdida de peso
- THR
- Embarazo
- Lactancia
- Cáncer inflamatorio
- Mastitis

Disminuyen la densidad

- Edad
- Menopausia
- Algunos medicamentos como el Danazol
- Vitamina D y el calcio en mujeres pre-menopáusicas
- Aumento de peso
- Acromegalia

Densidad mamaria y menopausia





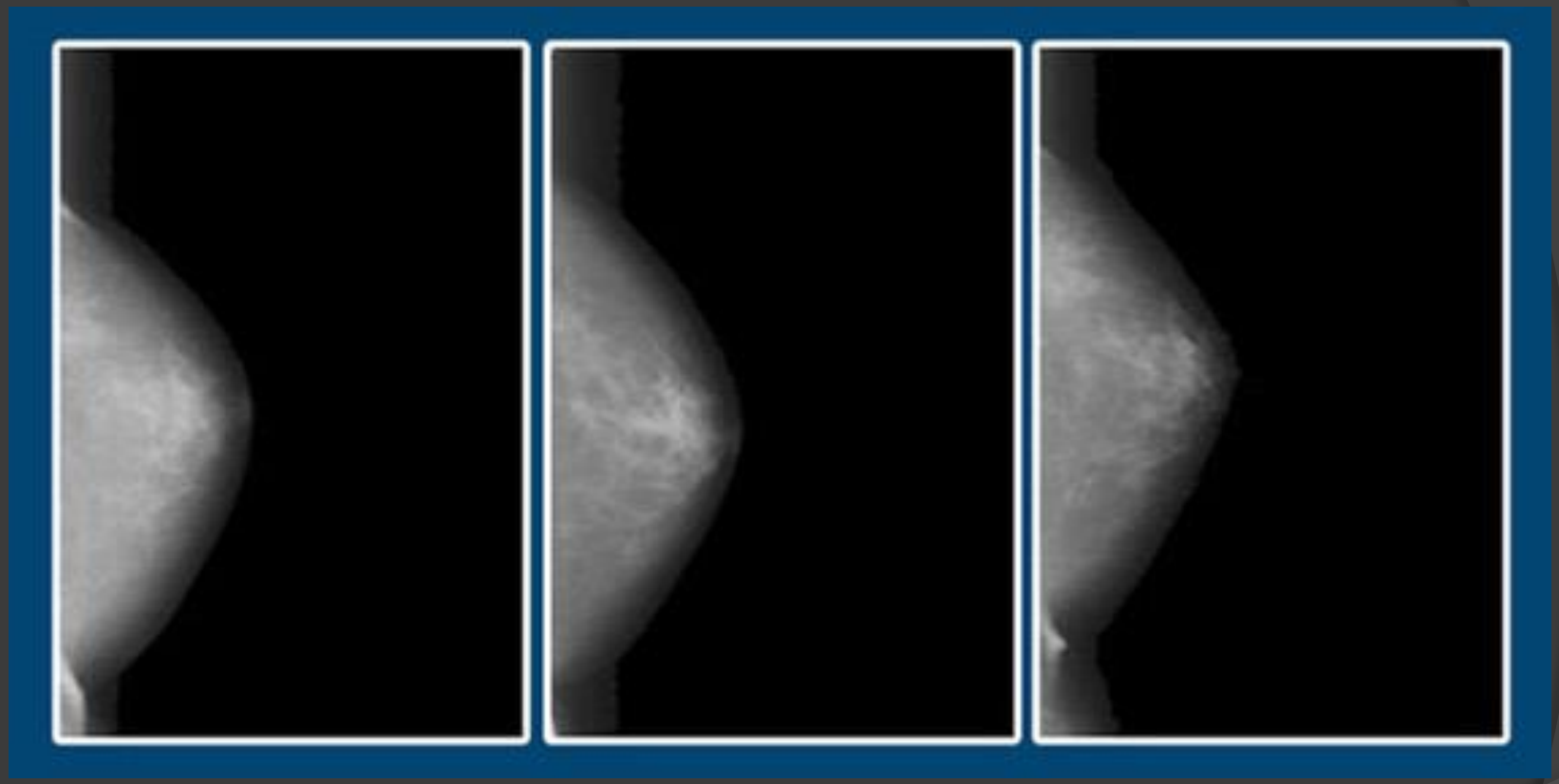
Mamografía y THR

- Las mujeres en tratamiento con THR tienen mas frecuentemente dolor y tensión en las mamas que dificulta la obtención de imágenes satisfactorias
- Menos frecuencia de antecedentes familiares
- Mayor frecuencia de síntomas asociados

Mamografía y THR

- La terapia hormonal de reemplazo con el uso prolongado aumenta la densidad glandular (aumenta el porcentaje de tejido fibroglandular)
- El aumento de la densidad es reversible con la suspensión de su uso durante 1 mes

High breast density in women using HT was correlated with greater fibrous stroma (P = 0.020) and lobule type 1 (P = 0.016). Breast density also correlated with Ki67 activity in the ducts (P = 0.031) and lobules (P= 0.023) for both groups combined. Estrogen and progesterone receptors did not correlate with either breast density or HT use. Harvey JA. Menopause. 2008 Jan-Feb;15(1):67-73



Changes in Breast Density Associated With Initiation, Discontinuation, and Continuing Use of Hormone Replacement Therapy

Carolyn M. Rutter, PhD
Margaret T. Mandelson, PhD
Mary B. Laya, MD
Deborah J. Seger
Stephen Taplin, MD

Context Initiation of hormone replacement therapy (HRT) has been shown to increase breast density. Evidence exists that increased breast density decreases mammographic sensitivity. The effects on breast density of discontinuing and continuing HRT have not been studied systematically.

Objective To examine the effects of initiation, discontinuation, and continued use of HRT on breast density in postmenopausal women.

Design, Setting, and Participants Observational cohort study of 5212 naturally postmenopausal women aged 40 to 96 years and enrolled in a large health maintenance organization in western Washington State who had 2 screening mammograms between 1996 and 1998.

Main Outcome Measures Breast density, assessed using the clinical radiologists' BI-RADS 4-point scale, compared among women who did not use HRT before either mammogram (nonusers); who used HRT before the first but not before the second mammogram (discontinuers); who used HRT before the second but not before the first mammogram (initiators); and who used HRT prior to both mammograms (continuing users).

Results Relative to nonusers, women who initiated HRT were more likely to show increases in breast density (relative risk [RR], 2.57; 95% confidence interval [CI], 2.12-3.08), while women who discontinued HRT use were more likely to show decreases in density (RR, 1.81; 95% CI, 1.06-2.98) and women who continued to use HRT were more likely to show both increases in density (RR, 1.33; 95% CI, 1.13-1.55) and sustained high density (RR, 1.45; 95% CI, 1.33-1.58).

Conclusions These results indicate that breast density changes associated with HRT are dynamic, increasing with initiation, and decreasing with discontinuation.

JAMA. 2001;285:171-176 www.jama.com

Mamografía y THR

¿La THR modifica la detección de cáncer de mamas por mamografía?

	Description of study	Screening interval (years)*	Sensitivity (%) (95% CI)	
			No HRT	HRT
Cohen and colleagues (1997)[14]	50–64 years, includes invasive cancers only, first-round and subsequent screening	2	82% (79–86)	71% (60–81)
Kavanagh and colleagues (2000, this paper)†	50–69 years, inclusive invasive cancers only, first-round screening	1	93% (91–96)	84% (77–90)
		2	80% (76–84)	64% (57–72)
Laya and colleagues (1996)[8]	50 years and older, includes DCIS and invasive cancers, first-round	1	94% (80–99)	69% (38–91)
Litherland and colleagues (1999)[13]	50–64 years (no details on whether DCIS included or which screening rounds)	1	96% (95–97)	90% (86–94)
		3	76% (73–78)	60% (53–68)
Rosenberg and colleagues (1998)[12]†	50–64 years, includes DCIS and invasive cancers, first-round and subsequent screening	1	83% (76–90)	68% (58–77)
Séradour and colleagues (1999)[11]	50–69 years, includes DCIS and invasive cancers, first-round and subsequent screening	1	93% (90–95)	71% (60–82)

DCIS=ductal carcinoma-in-situ. *Screening interval for sensitivity estimate. †These studies included a broader age range but only the results of wo[illegible] colleagues) and women aged 50–64 years (Rosenberg and colleagues) are presented, to enable comparison of the other studies.

Table 4: **Summary of studies on HRT use and sensitivity of screening mammography**

THE LANCET • Vol 355 • January 22, 2000

Hormone replacement therapy and accuracy of mammographic screening

Anne M Kavanagh, Heather Mitchell, Graham G Giles

Summary

Background Hormone replacement therapy (HRT) is commonly used and may affect the accuracy of mammographic screening.

Methods We examined the sensitivity, specificity, and small-cancer detection rate according to HRT use in 103 770 women in Victoria, Australia, who attended first-round screening in 1994 and who did not have a personal history of breast cancer or a breast lump or a bloodstained or watery nipple discharge at the time of screening. BreastScreen Victoria provides mammography to women aged 40 years and older every 2 years. Unconditional logistic modelling was used to adjust for age, family history, and symptom status.

Findings The sensitivity of screening mammography for a 2-year screening interval was lower in HRT users (64·8% [95% CI

Introduction

Whereas randomised controlled trials have shown reductions in breast-cancer mortality with mammographic screening,[1] it is recognised that mammographic-screening programmes can deliver a mortality benefit only if they achieve a high sensitivity and a high small-cancer detection rate. Furthermore, breast-cancer screening can be cost-effective only if it has a high specificity.

The accuracy of screening mammography has been shown to vary with age[2–5] mammographic density,[6,7] and family history of breast cancer.[2,3] Studies have also shown that use of hormone replacement therapy (HRT) may be associated with a reduction in the specificity of screening mammography.[8–11] Several studies have also reported a reduction in sensitivity with HRT use,[8,11,14] whereas another failed to show this effect.[10]

Any effect of HRT use on how screening mammography

Hormone replacement therapy and accuracy of mammographic screening

Anne M Kavanagh, Heather Mitchell, Graham G Giles

- Investigaron el efecto de la THR en la sensibilidad y especificidad de la mamografía y el número de cánceres pequeños detectados en el screening
- 103770 mujeres, mayores de 40 años, Victoria, Australia
- 1° mamografía de screening
- Control a los 24 meses
- Sin antecedentes familiares, hallazgos clínicos o descarga por pezón

Hormone replacement therapy and accuracy of mammographic screening

Anne M Kavanagh, Heather Mitchell, Graham G Giles

Resultados

- La sensibilidad de la mamografía de screening fue menor en pacientes con HRT (64.8%) con respecto de pacientes sin HRT (77.3%).
- Entre las pacientes que tuvieron cáncer del intervalo las tratadas con HTR tuvieron mayor riesgo de falsos negativos

Hormone replacement therapy and accuracy of mammographic screening

Anne M Kavanagh, Heather Mitchell, Graham G Giles

Resultados

- La especificidad fue 0.6% menor en pacientes con HTR con respecto a no tratadas
- Entre las pacientes que no tuvieron cáncer del intervalo, las usuarias estuvieron más expuestas a resultados falso positivos

Hormone replacement therapy and accuracy of mammographic screening

Anne M Kavanagh, Heather Mitchell, Graham G Giles

Algunos aspectos

La disminución en la sensibilidad y especificidad podría estar ligada al aumento de la densidad

El mayor impacto esta demostrado en pacientes con mamas densas que reciben HTR

La terapia combinada es la que determina mayor aumento de la densidad

Hormone replacement therapy and accuracy of mammographic screening

Anne M Kavanagh, Heather Mitchell, Graham G Giles

Algunos aspectos

No encontraron evidencias en favor de la teoría que sostiene que hay un crecimiento tumoral mayor en pacientes con HTR

Hormone replacement therapy and accuracy of mammographic screening

Anne M Kavanagh, Heather Mitchell, Graham G Giles

Recomendación

Informar a las pacientes del riesgo del uso de THR y su impacto en los hallazgos mamográficos

Suspender por un periodo de tiempo de 2 semanas a un mes, previo a la realización de la mamografía

Densidad mamaria y tipo de THR

ARTICLES

Postmenopausal Hormone Therapy and Change in Mammographic Density

Gail A. Greendale, Beth A. Reboussin, Stacey Slone, Carol Wasilauskas, Malcolm C. Pike, Giske Ursin

Background: **Mammographic density is an independent risk factor for breast cancer. Postmenopausal hormone use is associated with an increase in mammographic density, but the magnitude of the density increase is unknown.** ***Methods:*** **Baseline and 12-month mammograms were obtained for 571 (65%) of the 875 women, aged 45–64 years, who were enrolled in the Postmenopausal Estrogen/Progestin Interventions Trial and randomly assigned to receive placebo, daily conjugated equine estrogens at 0.625 mg/day (CEE), daily CEE and medroxyprogesterone acetate (MPA) at 10 mg/day on days 1–12 (CEE+MPA-cyclic), daily CEE and MPA at 2.5 mg/day (CEE+MPA-continuous), or daily CEE and micronized progesterone (MP) at 200 mg/day on days 1–12 (CEE+MP). We analyzed digitized mammograms to determine the percentage of the left breast that was composed of dense tissue (i.e., mammographic percent density). Linear regression analysis was used to examine the effects of treatments on the change in mammographic percent density between baseline and 12 months, before and after adjustment for possible confounders. All statistical tests were two-sided.**

–0.07% (95% CI = –1.50% to 1.38%). ***Conclusion:*** **Greater mammographic density was associated with the use of estrogen/progestin combination therapy, regardless of how the progestin was given, but not with the use of estrogen only. [J Natl Cancer Inst 2003;95:30–7]**

IRM y THR

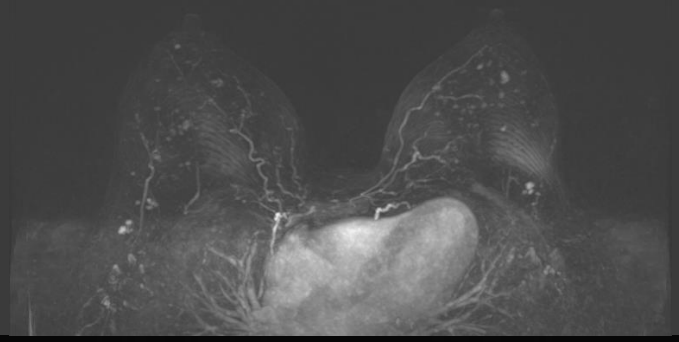
Cuando evaluamos una paciente con IRM mamaria tenemos en cuenta dos aspectos:

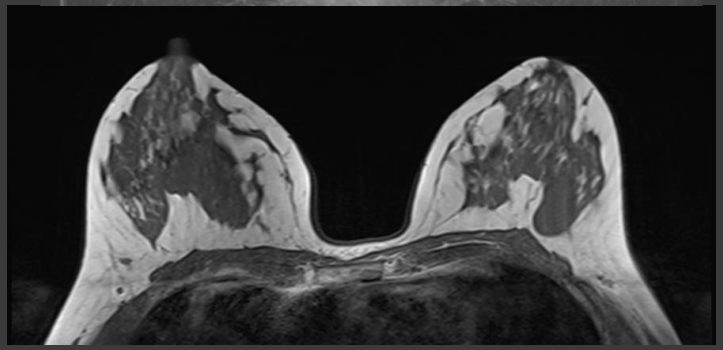
- Cantidad de tejido fibroglandular
- Realce parenquimatoso de fondo

IRM y THR

- Porcentaje de tejido fibroglandular
  ➡ buena correlación con la densidad mamográfica (Wei et al 2006)

- Realce parenquimatoso de fondo
  ➡ se correlaciona con la proliferación epitelial estimulada por la progesterona





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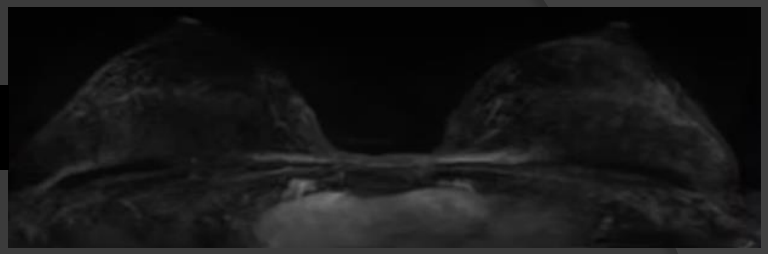

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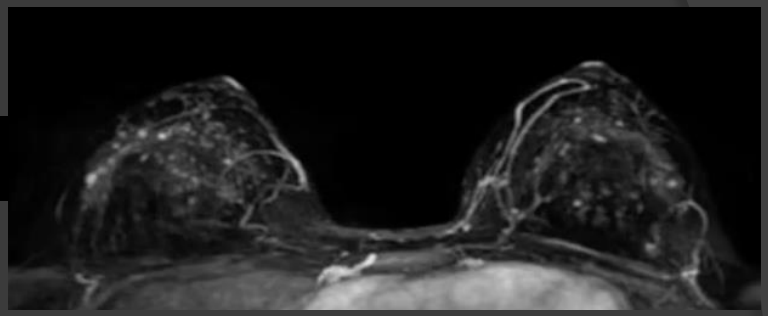

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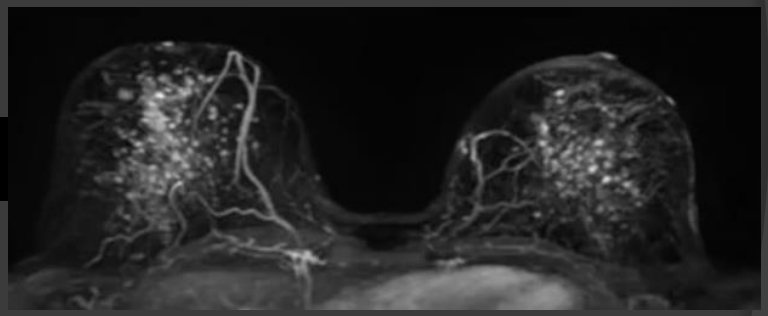

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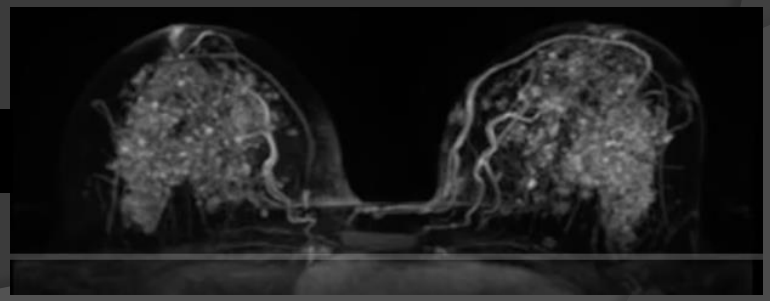


IRM y menopausia

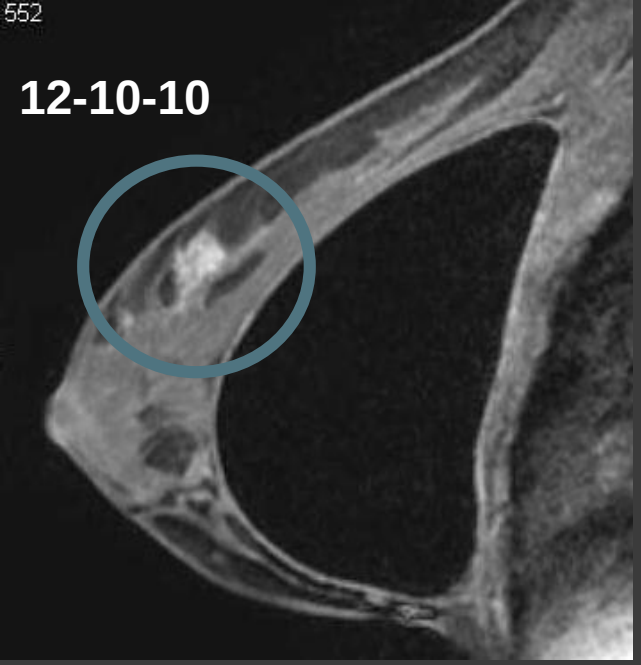
European Radiology
December 2012, Volume 22, Issue 12, pp 2641–2647

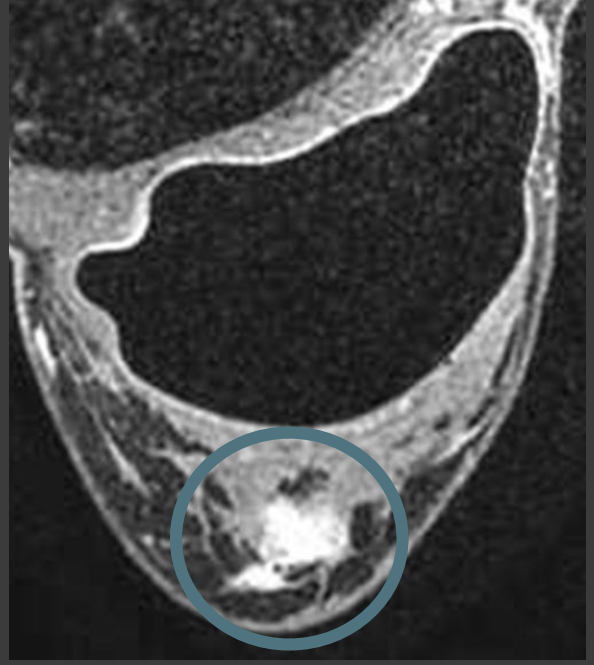
Impact of menopausal status on background parenchymal enhancement and fibroglandular tissue on breast MRI

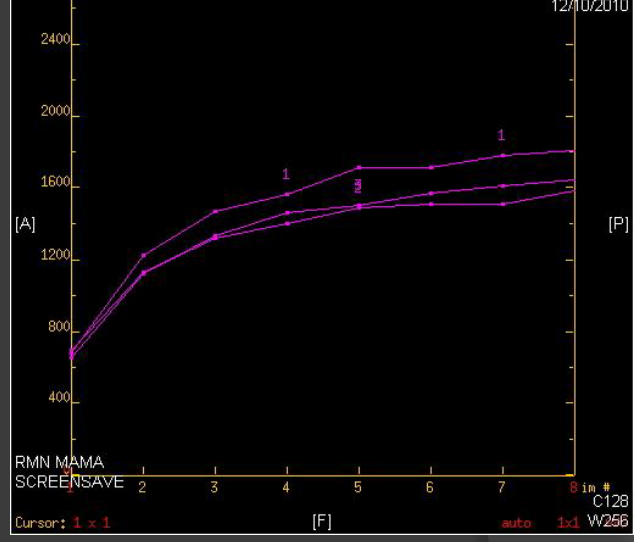
	=	⇩
Realce de fondo	39%	61%
Tejido fibroglandular	61%	39%

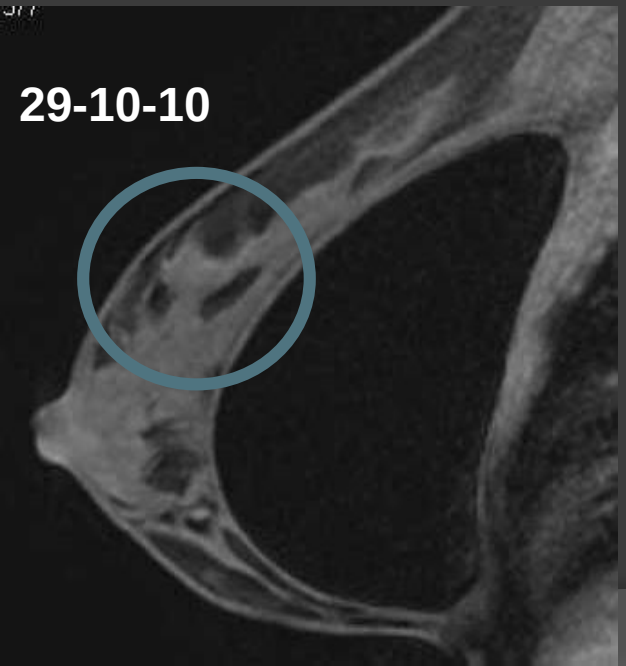
IRM y THR

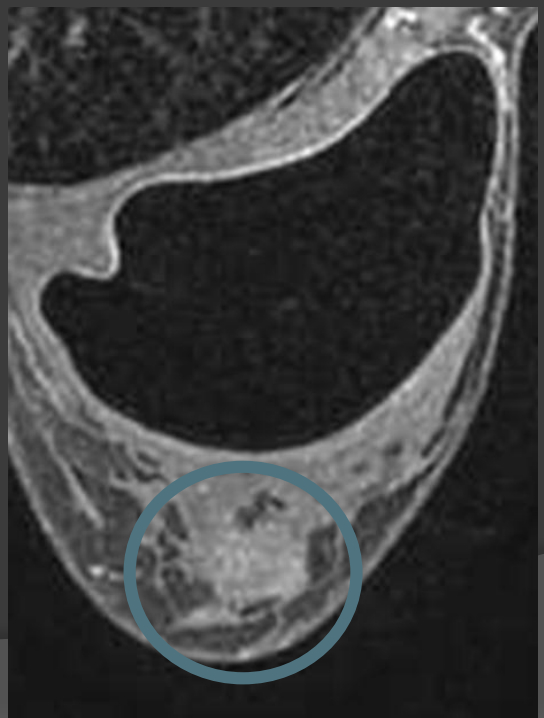
- La THR induce un aumento de la perfusión del parénquima glandular
- Aumenta el realce de fondo
- La THR puede inducir realce de aspecto anormal en las secuencias post inyección de gadolinio
- La terapia combinada es la que determina mayor realce → ligada al estimulo de proliferación celular asociada con la progesterona
- En casos de duda se sugiere repetir IRM entre 2 y 4 semanas después de la suspensión del tratamiento





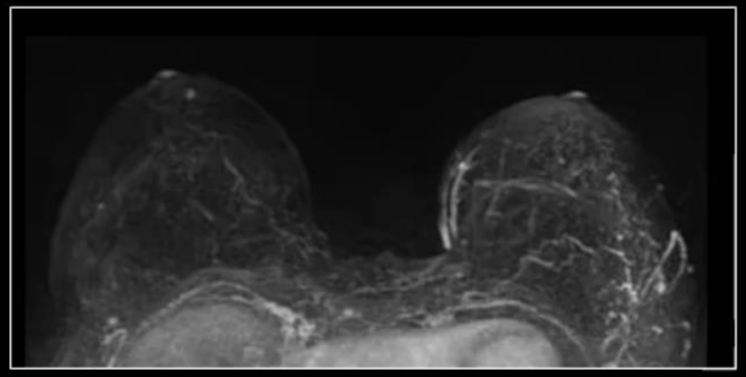






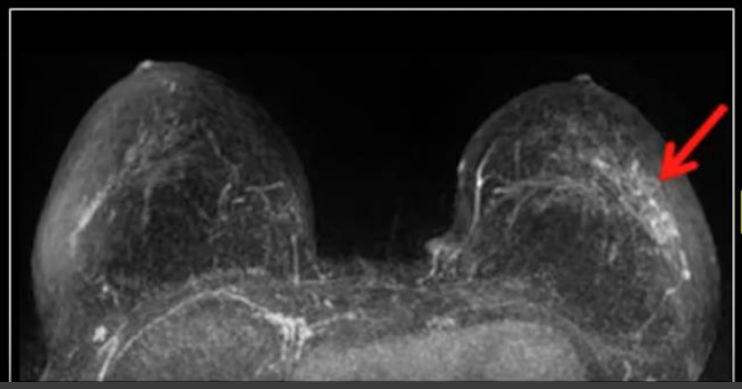
Gentileza Dr J Rodriguez Lucero Rosario

Examen en Agosto/2011

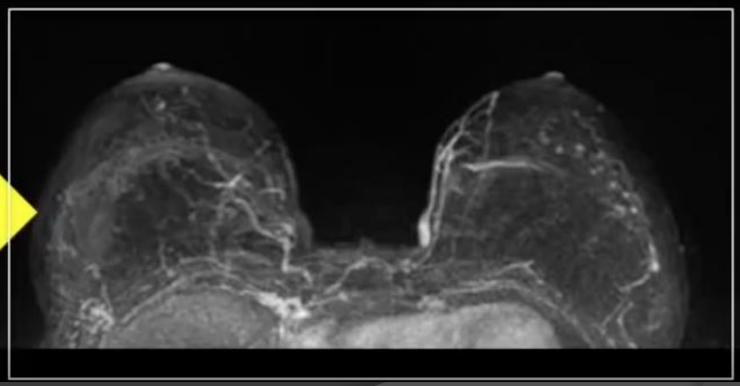


62 años, en seguimiento por prótesis desde hace 13 años

Examen en Mayo/2012



Retorna después de 2 meses de interrupción del TRH:



Conclusiones

- La THR, aumenta el volumen de tejido fibroglandular → aumento de la densidad del paréquima en mamografía → ↓ de la sensibilidad y especificidad de la mamografía de screening
- Los cambios descriptos son reversibles con la suspensión de la medicación
- Igual impacto de observa en la IRM → RPF
- Es indispensable evaluar los costos - beneficios de la misma

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