



From Research to Practice: Training in Reproductive Health Research WHO 16 March 2006, Geneva

Dynamic angiothermography

*A new technology for breast cancer
screening and diagnosis*

*Prof. Gian Carlo Montruccoli
Prof. Daniele Montruccoli*

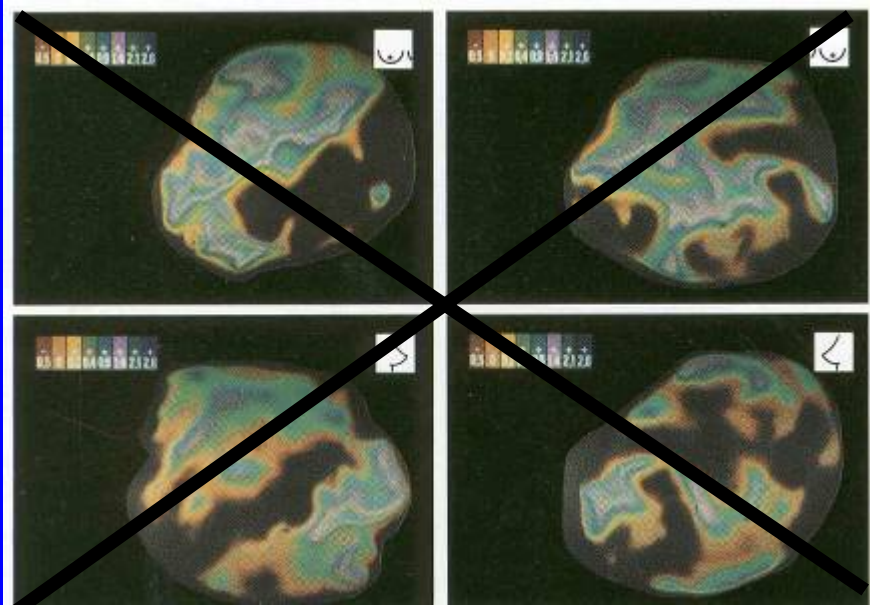
Geneva Foundation
for Medical Education and Research



Dynamic Angiothermography (DATG)

- New functional diagnostic tool
- Based on the imaging of mammary gland's normal vascularization and detection of its angiogenetic micro-circulation
- Morphological, qualitative images of the breast's functional blood supply
- Reproducible, non-invasive
- R&D with Dept Medical Physics, University of Bologna
- Clinical results for 7000 patients, 25-year follow up
- Excellent integration with other breast diagnostic techniques

QUANTITATIVE vs. QUALITATIVE



Old Contact Thermography

- Quantitative method
- based on the measurement of thermal gradients (ΔT) evaluated by image coloration



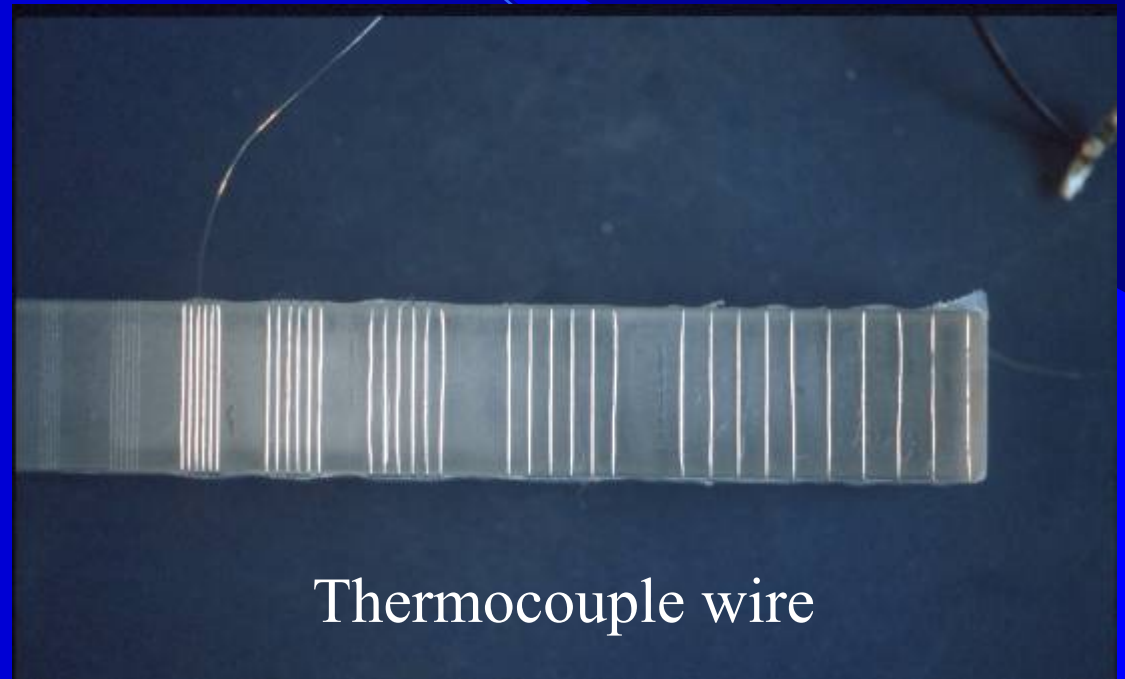
Dynamic Angiothermography -DATG

- Qualitative method
- based on the detailed patterns of functional blood flows

TEST 1



- Experiments run at the University of Bologna's Department of Physics tested the plate against the others on the market, especially as to spatial resolution (as high as a tenth of a millimeter) and response time. The results were excellent and the plate has now been patented in Europe and the United States.



Thermocouple wire

From: "A new type of breast contact thermography plate: a preliminary and qualitative investigation of its potentiality on phantoms"-

Physica Medica- (Vol. XX, N. 1 January-March 2004 pp.27-31)

TEST 1

spatial resolution (as high as a tenth of a millimeter)

Separate
lines

Our plate

TEST 1 A

Lines not
separate

Commercial plate

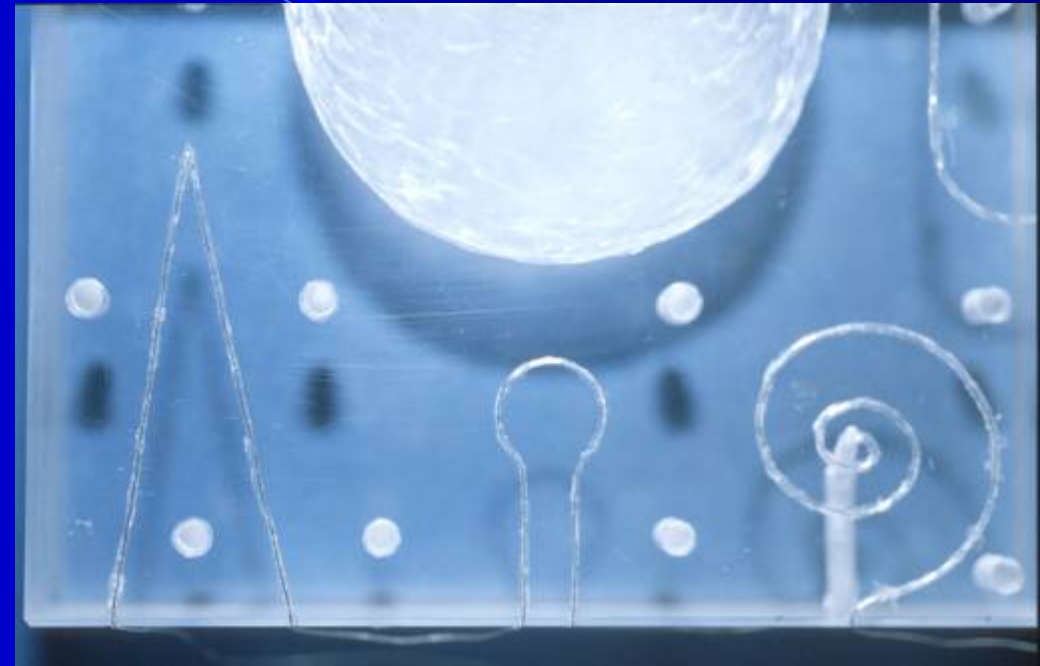
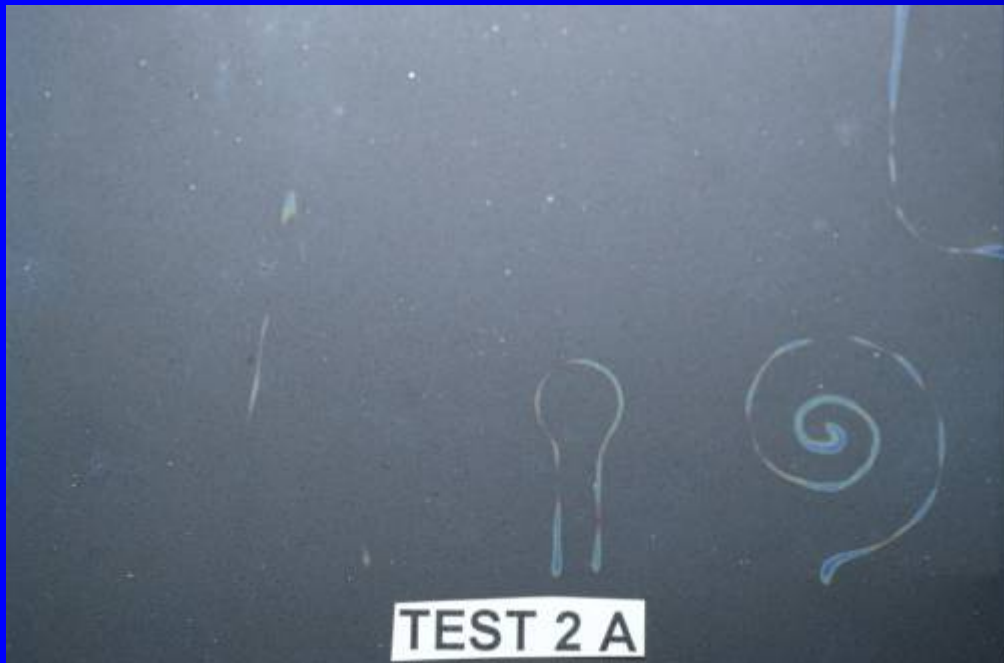
TEST 1 B

From: "A new type of breast contact thermography plate: a preliminary and qualitative investigation of its potentiality on phantoms"-

Physica Medica- (Vol. XX , N. 1 January-March 2004 pp.27-31)

TEST 2A after 3''

response time



University of Bologna's Department of Physics

From: "A new type of breast contact thermography plate: a preliminary and qualitative investigation of its potentiality on phantoms"-

Physica Medica- (Vol. XX , N. 1 January-March 2004 pp.27-31)

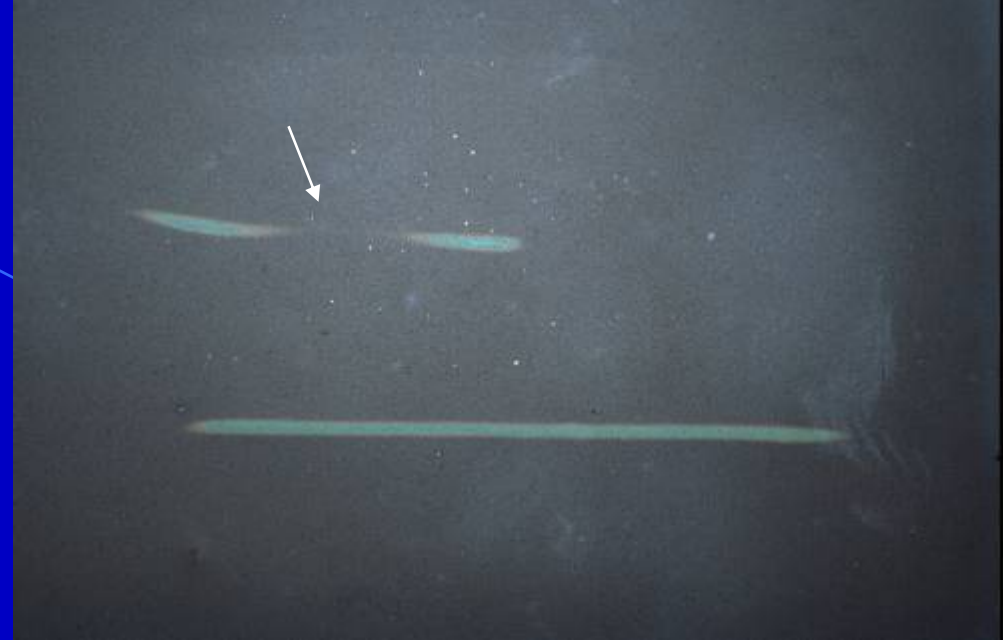


Plate sensitivity

- We tried to reproduce blood flow lines in Dep. of Physics
- Insertion of the tube with warm water into the wax phantom
- Pointed terminations (normal flow lines)

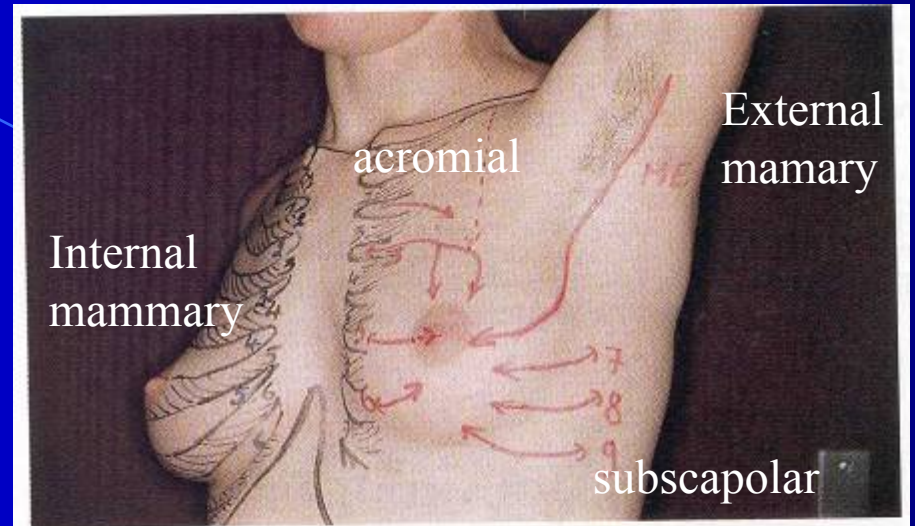
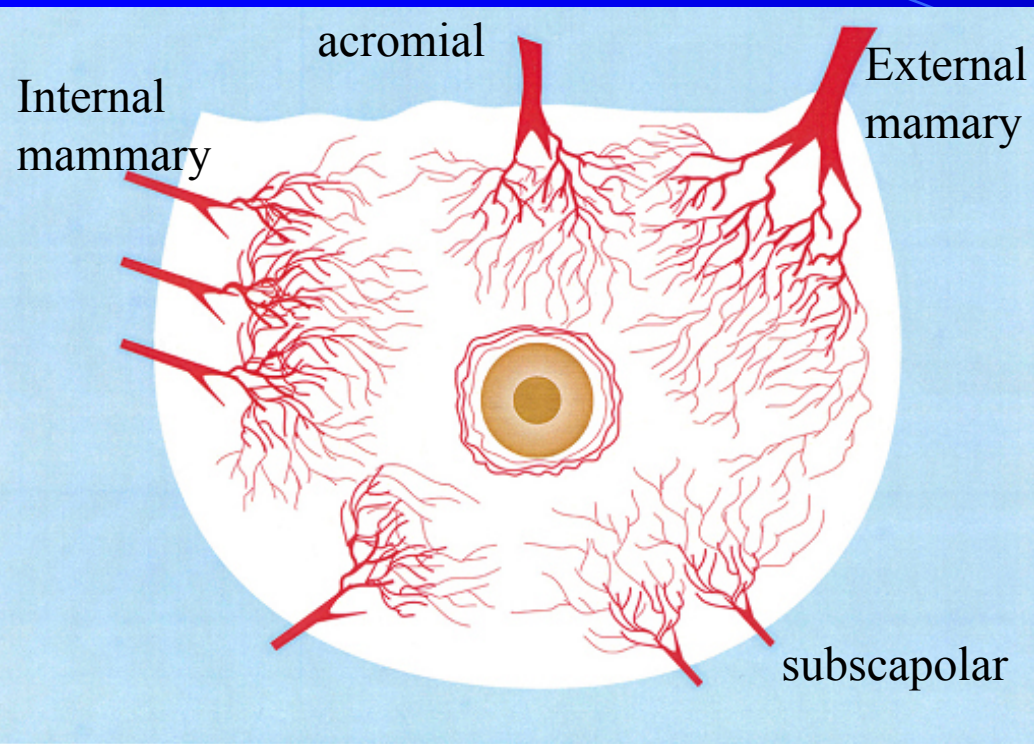


Fig. 5. — Axes artériels dessinés suivant leur projection cutanée sur une glande mammaire normale.

Fig. 5. — Arteries drawn according to their cutaneous projection on the normal breast.

➤ Scheme of vascular anatomy of left breast

➤ Cutaneous projection of the breast's main arteries.

DATG in clinic



First you cool the skin to remove any background noise



Fig. 8. — Dissection anatomique après injection de résine autopolymérisable intra-artérielle : mise en évidence de l'artère mammaire externe de type I majeur.

Fig. 8. — Anatomical dissection after intra-arterial injection of autopolymerizable resin : demonstration of a major type I external mammary artery.



Normal flowlines

DATG

Normal angiothermographics flowlines reproduce the anatomy of the circulation of the breast

➤ The flow-lines of each plexus should be centripetal, fade out as they terminate in their own area and be proportional to the contralateral.

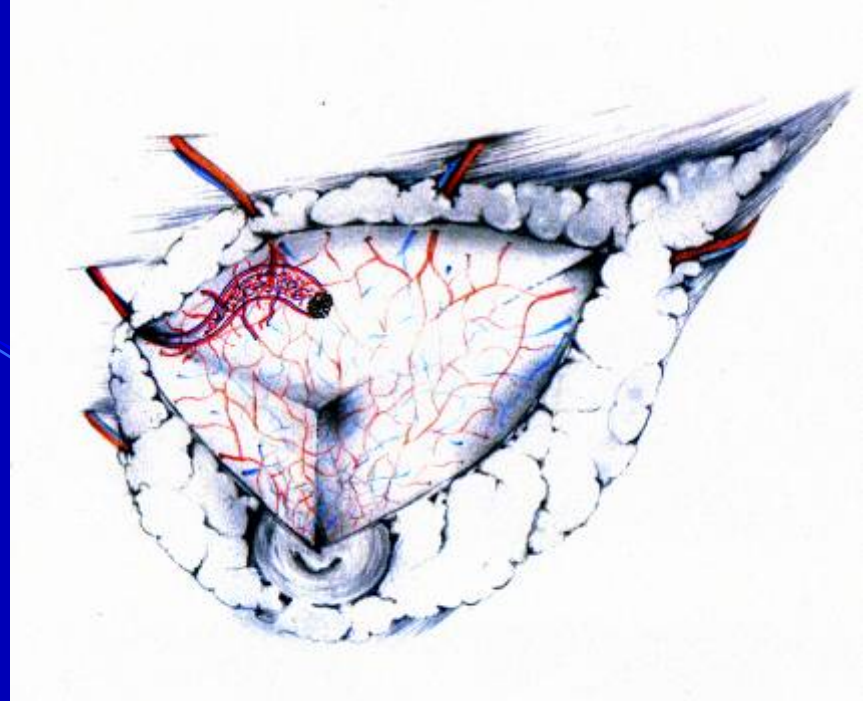


Fig. 10. — Dissection anatomique de l'artère acromio-thoracique après injection au latex : ici apparaît sa composante postérieure musculaire à destinée glandulo-cutanée (flèches rouges). La flèche noire indique l'origine de l'artère).

Fig. 10. — Anatomical dissection of the acromiothoracic artery after injection of latex, showing its posterior muscular component supplying the gland and the skin (arrows).



DATG



Upper internal quadrant of the left breast showing a marked anomalous flow line formed by countless vessels activated by a Lobular and Ductal Carcinoma in Situ with intraductal diffusion.

ID.3. n. 87

Frammento di tessuto fibro-adiposo, riferibile a parenchima mammario, misurante cm 8 di asse maggiore.
 Al taglio appare costituito da un tessuto bianco-roseo, nodulare.

Ax3
 Em4
 Cx3
 Dx3

13 prelievi random

Diagnosi:

Piccoli multipli di carcinoma lobulare in situ con diffusi aspetti di diffusione intraduttale a tipo "pagetoid spreading".

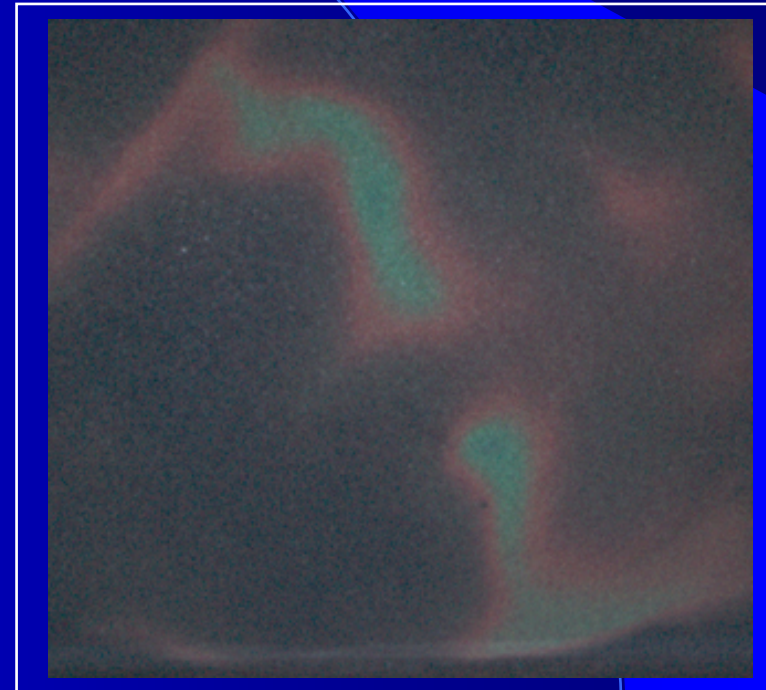
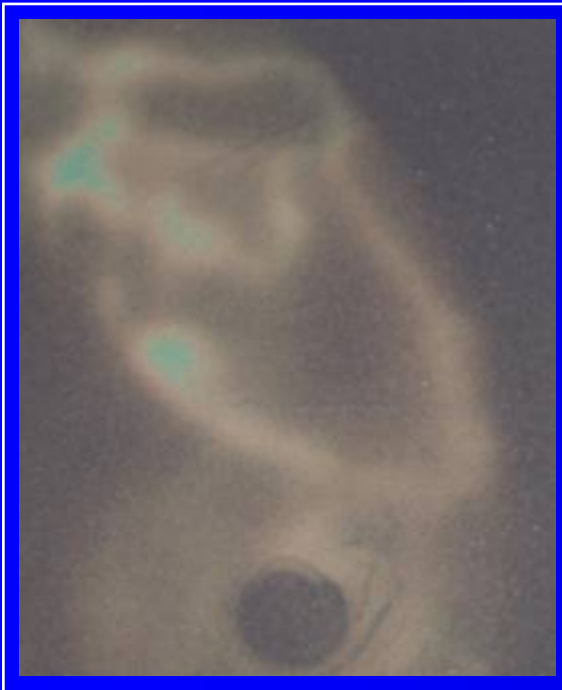
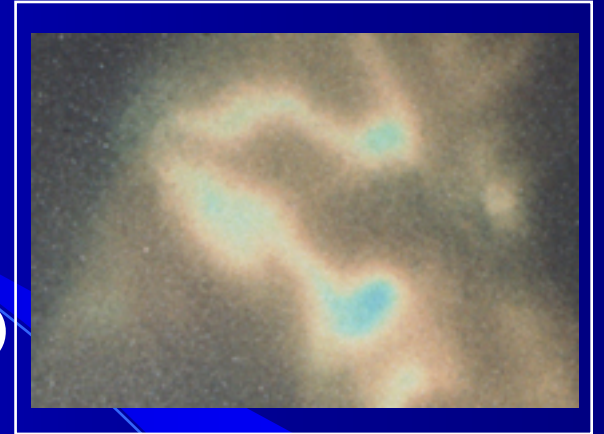
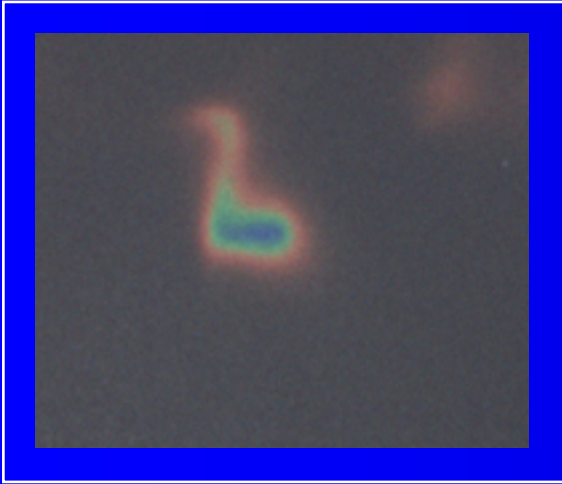
Il Responsabile
 del Laboratorio

PER CONFERENZA
 PROF. W.F. GRIGNONI

Histological report

SUSPICIOUS FLOWLINES

- Deviations (all)
- Non-pointed terminations (all)
- Flowlines that go beyond their own territory

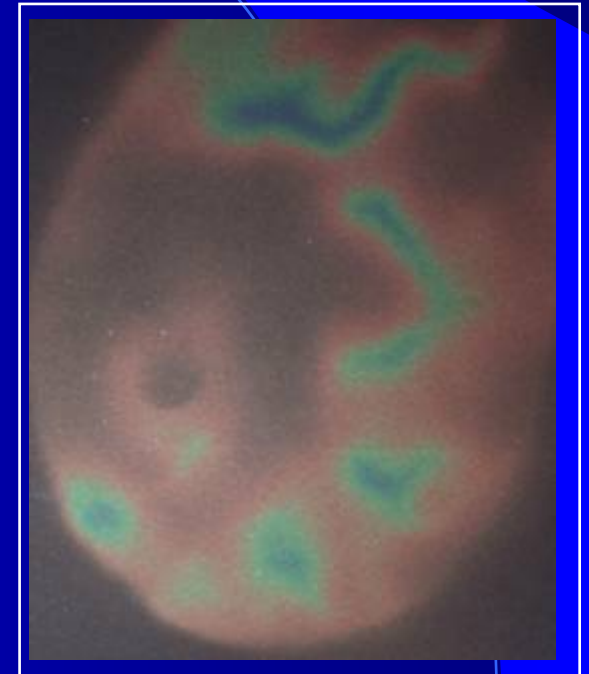
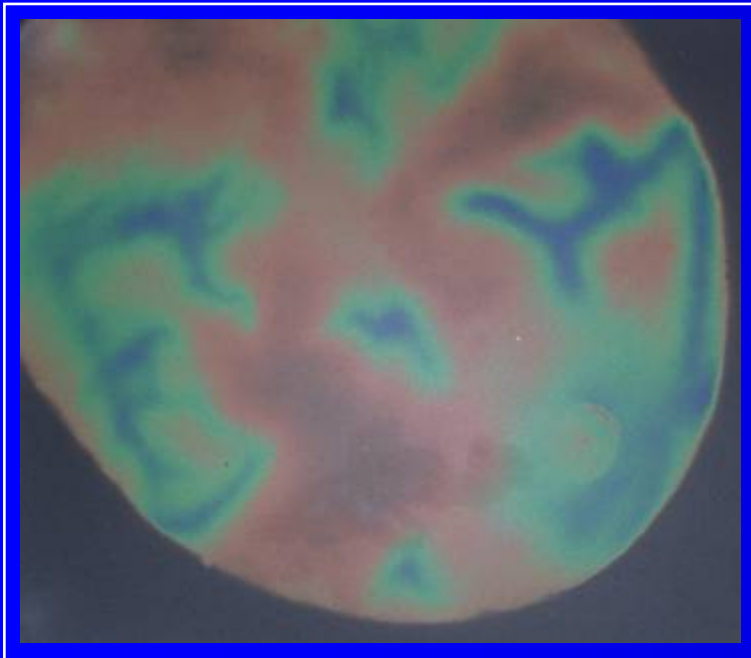
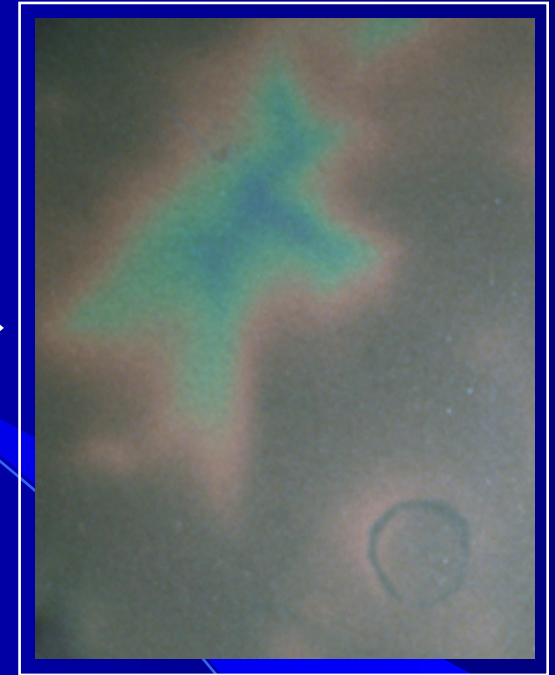


MALIGNANT FLOWLINES

• Two or more flowlines that cross one another: these are called malignant crosses or stars

• Flowlines that converge towards a central hotspot

• Flowlines that converge from different territories



- Menopausal patient

- «Malignant star»

- Infiltrating Lobular Carcinoma



- Biopsy zone

Mammography:
no pathological findings

The lesion is between skin and muscle perpendicular to the end of the angiothermographic flow line.

Diagnosi:

Carcinoma lobulare multifocale classico infiltrante associato a focolai di carcinoma lobulare in situ.

LCIS in pregnancy (8 weeks)

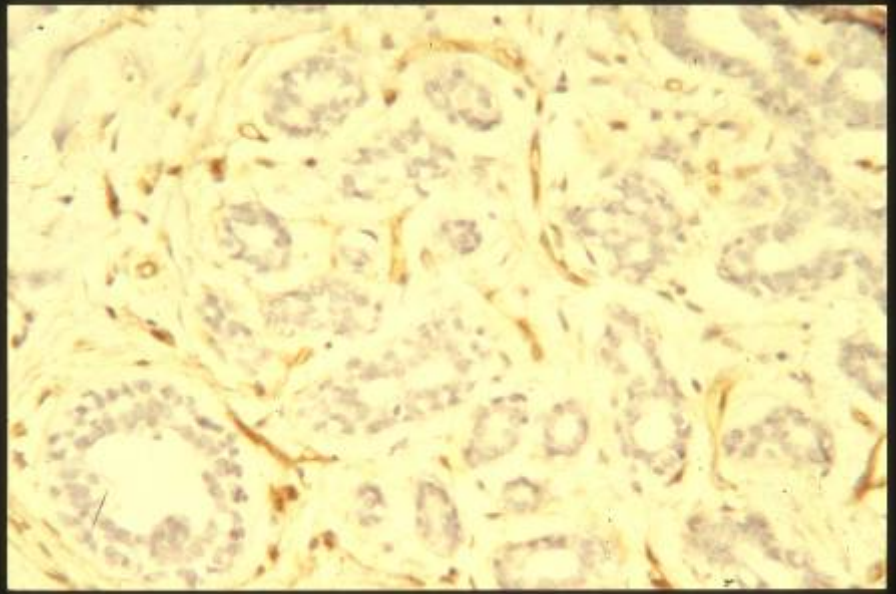


Ultrasound normal

Breast Cancer in Family:
Mother tested positive
one year later

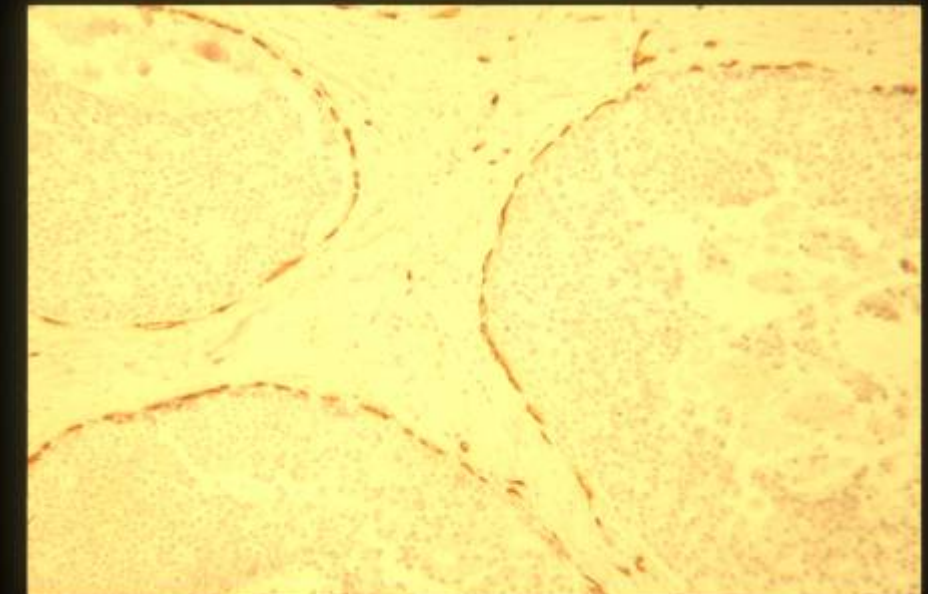
36 years old

- This 36-year-old patient, who said she was 8 weeks' pregnant, can have the angiotest because it is harmless.
- The check-up showed a hot spot with flow lines from the acromial and the external mammary in the upper left external quadrant.
- An ultrasound was negative but the biopsy, performed under local anesthetics, returned LCIS as the histological result.



Normal

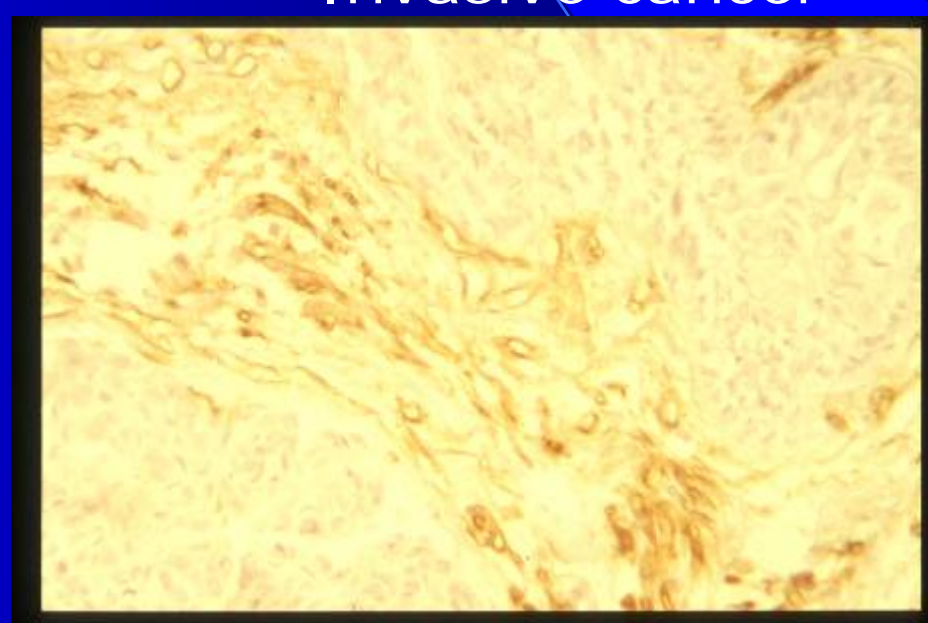
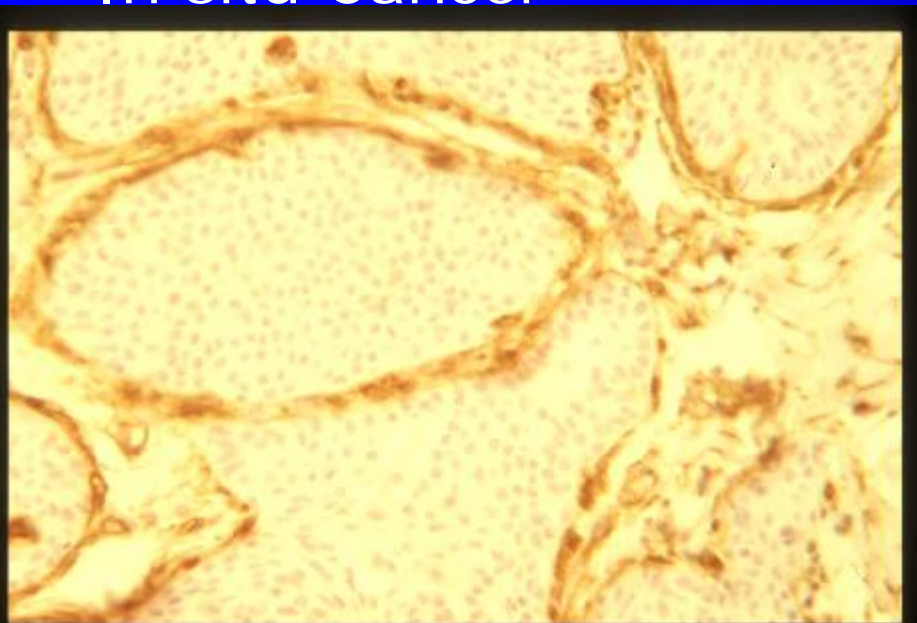
In situ Cancer



Hyperplasia

Progression of angiogenesis

Invasive cancer



Gro up	Histological diagnosis	No.	%	% group
A.	1. Benign	143	13.9	31.4
	2. Mastitis and/or ectasia	180	17.5	
B.	3. Simple ductal hyperplasia	169	16.45	39.33
	4. Florid ductal hyperplasia	235	22.88	
C.	5. Papillomatosis	46	4.47	4.47
D.	6. Atypical duct hyperplasia	7	0.68	4.2
	7. Atypical lobular hyperplasia	23	2.23	
	8. Mixed atypical hyperplasia	13	1.26	
E.	9. Ductal carcinoma in situ	15	1.46	5.56
	10. Lobular carcinoma in situ	28	2.72	
	11. Mixed carcinoma in situ	15	1.46	
F.	12. Ductal microinvasive carcinoma	2	0.19	0.9
	13. Lobular microinvasive carcinoma	5	0.48	
	14. Mixed microinvasive carcinoma	2	0.19	
G.	15. Ductal invasive carcinoma	123	11.97	13.83
	16. Lobular invasive carcinoma	15	1.46	
	17. Mixed invasive carcinoma	4	0.38	
H.	Malignant phyllodes	2	0.19	0.19
	TOTAL	1027		

Histological findings

❑ We performed 1,027 biopsies on 536 out of a total 6,568 patients from 1975 to 2001.

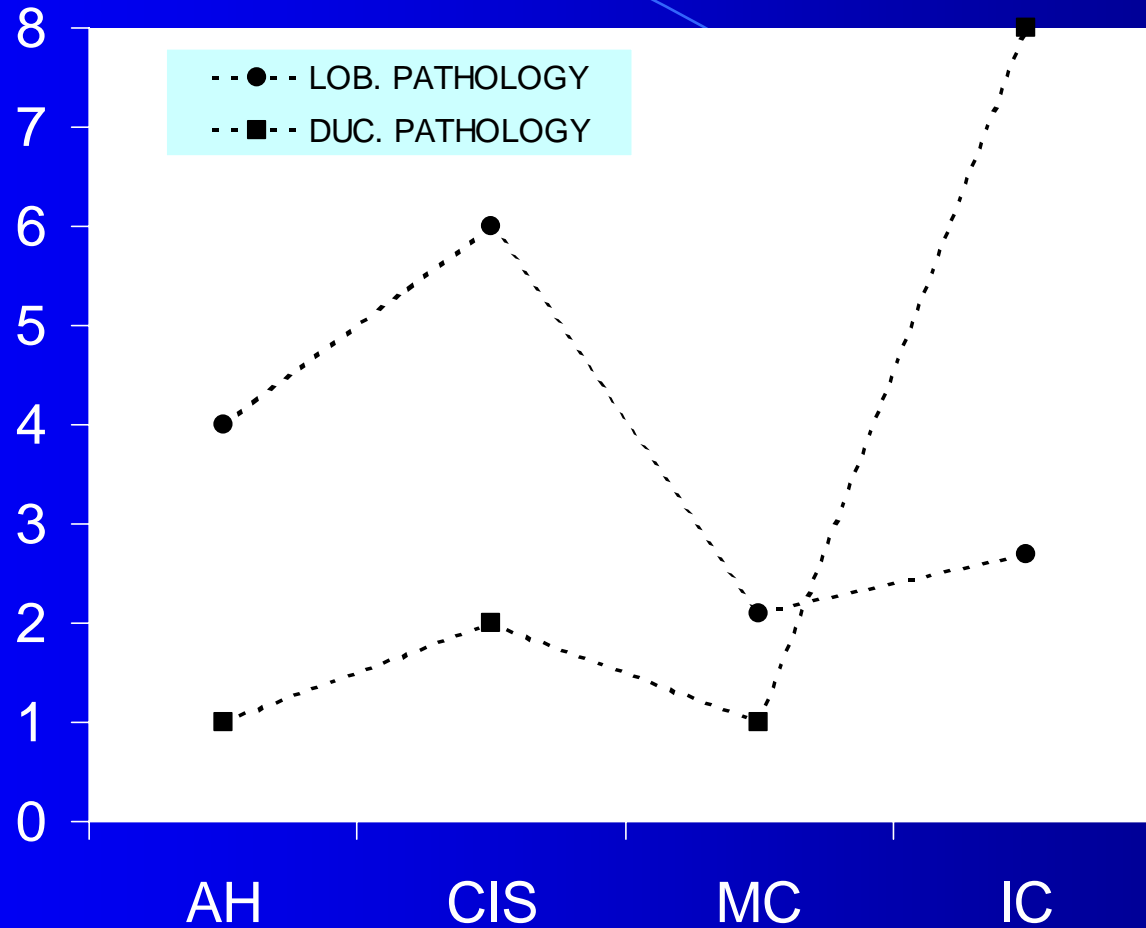
❑ Note first that the rate of epithelial lesions runs as high 70% if simple hyperplasia is considered.

(Molecular tests showed a loss of heterozygosity in 90% of hyperplasia cases)

❑ Note too that pre-invasive lobular lesions were more than double the ductal, contrary to what is reported in literature. This can be explained by the lobule's greater vascularisation with respect to the duct.

DATG-detected Lobular and Ductal Pathology

Number of cases



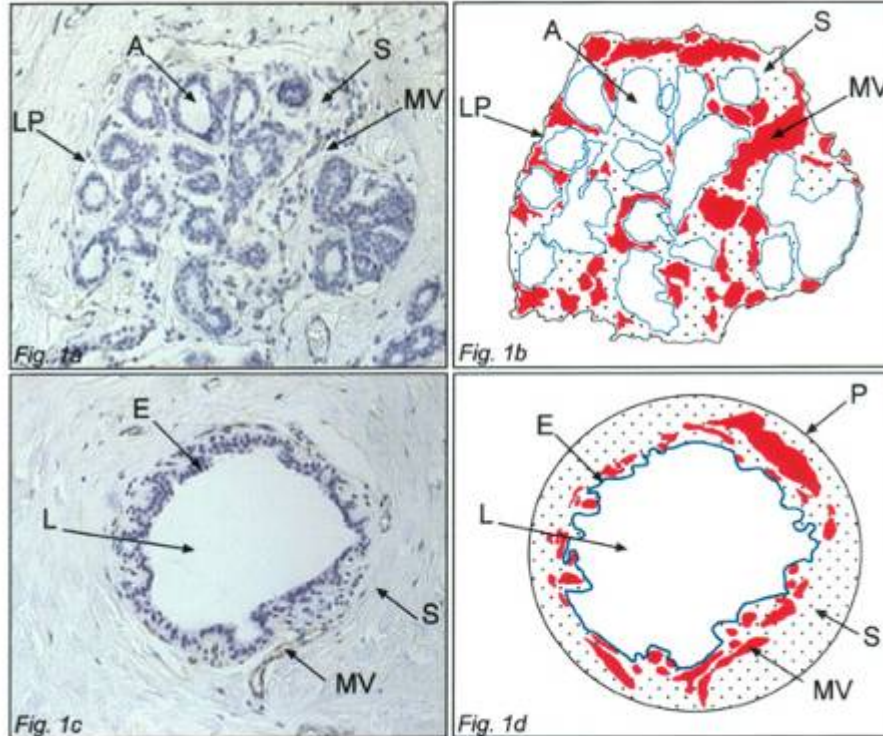
AH: ATYPICAL HYPERPLASIA; CIS: CANCER IN SITU;
MC: MICROINVASIVE CANCER; IC: INVASIVE CANCER

Microcirculation

“Naccarato A.G., Viacava P., Bocci G, Fanelli G., Lonobile A, Montruccoli G.C., and Bevilacqua G.

Definition of the microvascular pattern of the normal human adult mammary gland.

Journal of Anatomy
vol. 203, pp. 599-603,
2003”



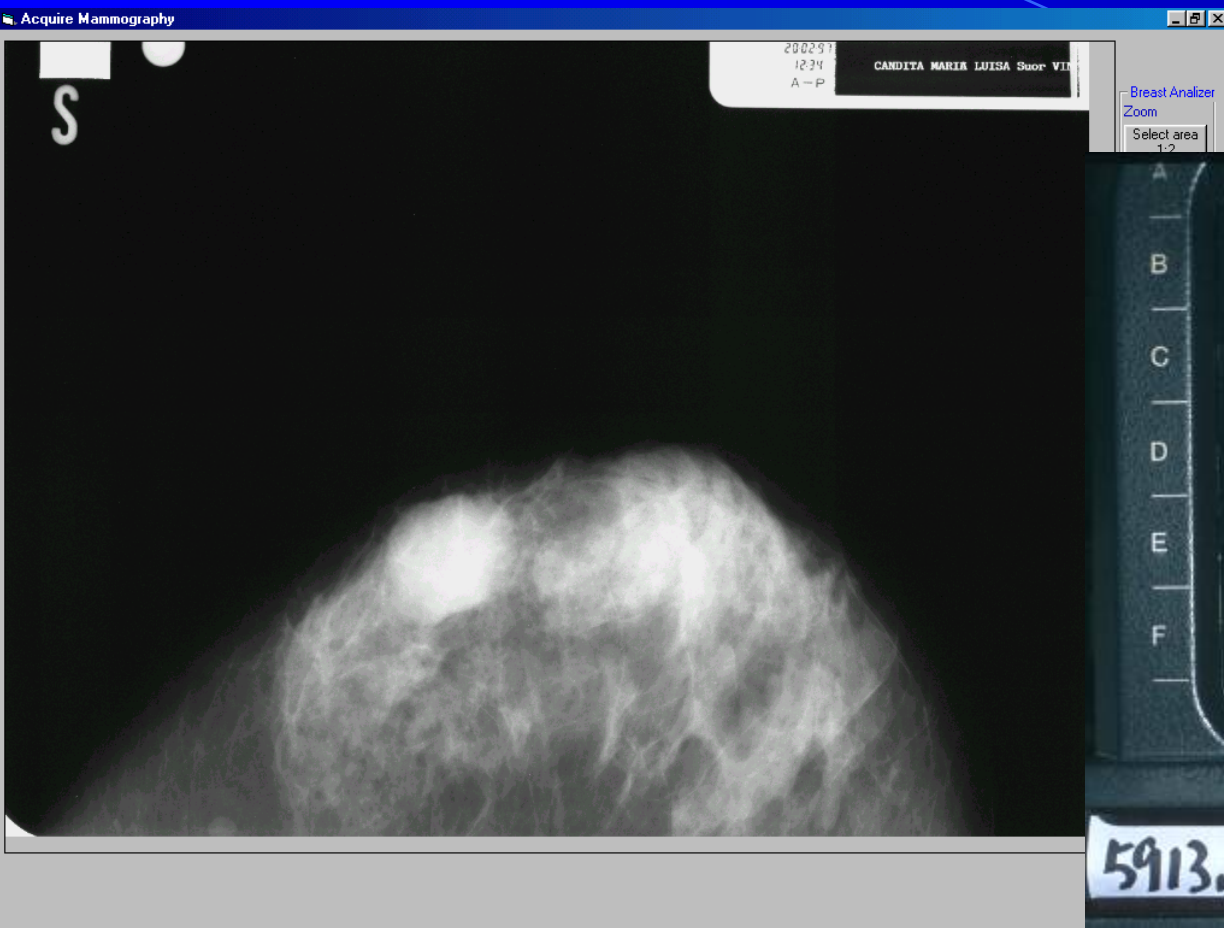
One finding in particular indicates that in the normal state the duct's microcirculation has a smaller surface area than the lobule's and that the latter's circulation is represented by sinusoids and is hence notably slower.

THREE FUNDAMENTAL CHARACTERISTICS OF DATG

- Each woman has her own strictly personal flowline pattern (like fingerprint)
- This personal pattern remains constant over decades in the absence of pathophysiological changes
- Pathological modifications are independent of tumor size and shape

Comparison of Diagnostic Techniques

5913

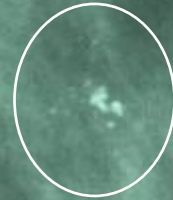


● 5913 Mammography 20-2-97

● 5913 left lateral 31-12-96

Pt 6128

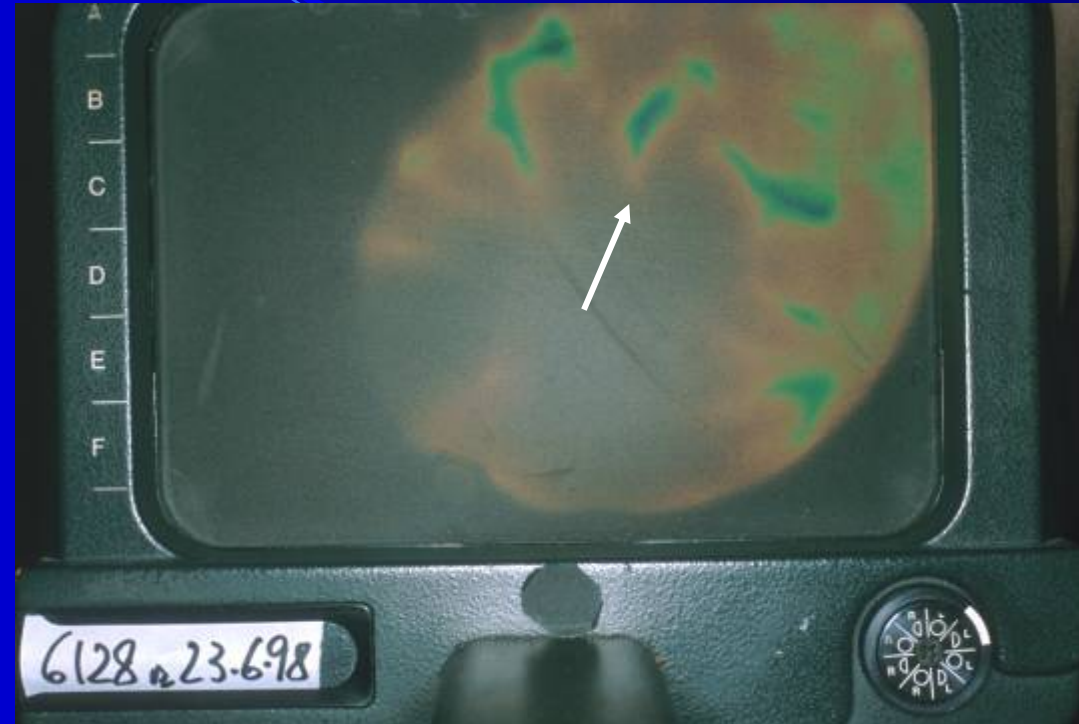
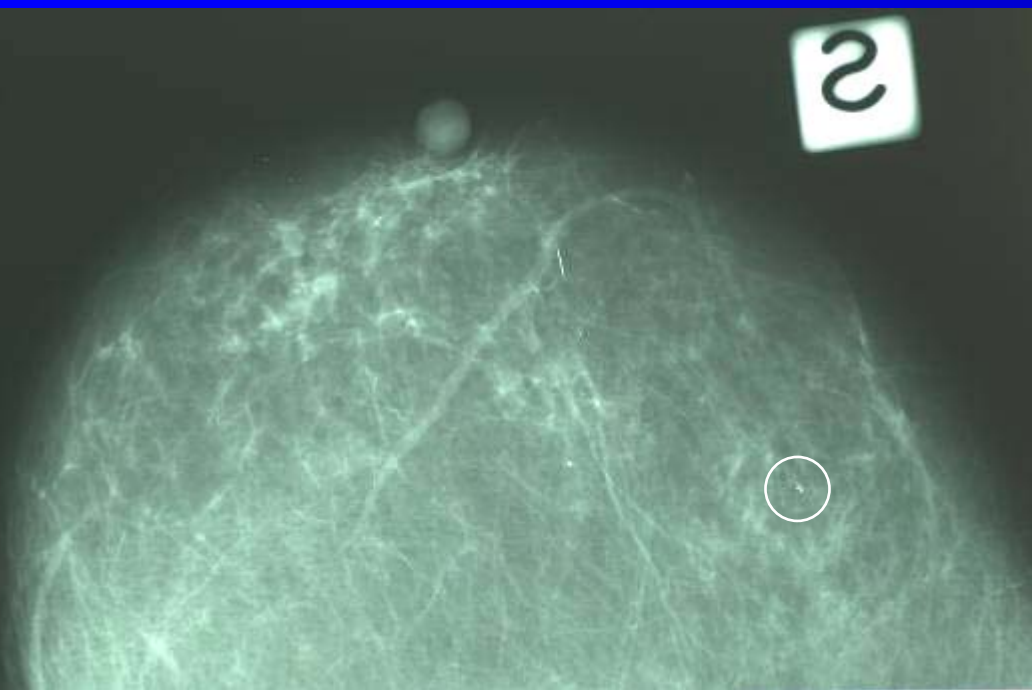
Appearance of microcalcifications :LCIS 3 mm.



MAMMOGRAPHY LEFT 2-6-1998 MICROCALCIFICATIONS

Pt 6128

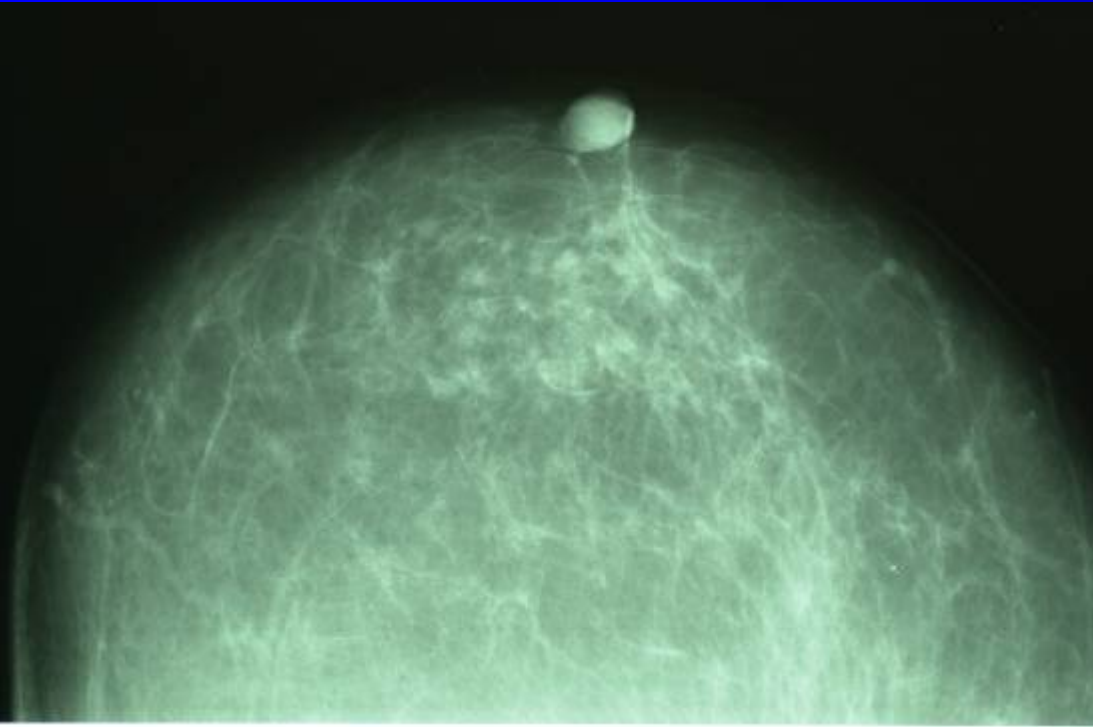
Appearance of microcalcifications :LCIS 3 mm.



● MAMMOGRAPHY LEFT 2-6-1998

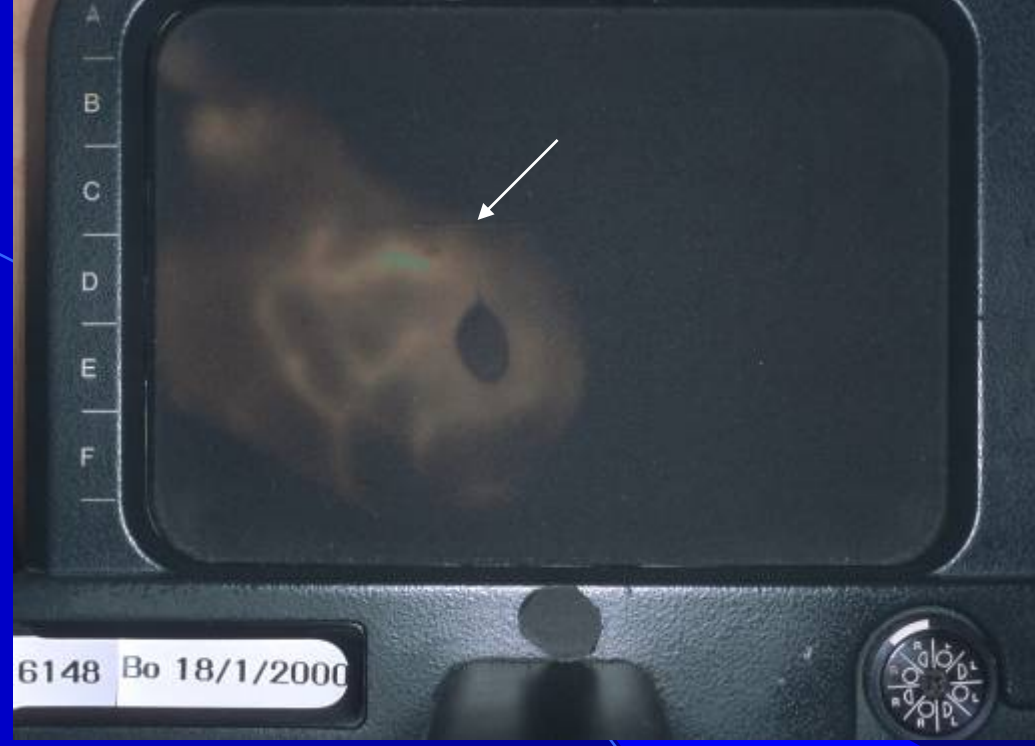
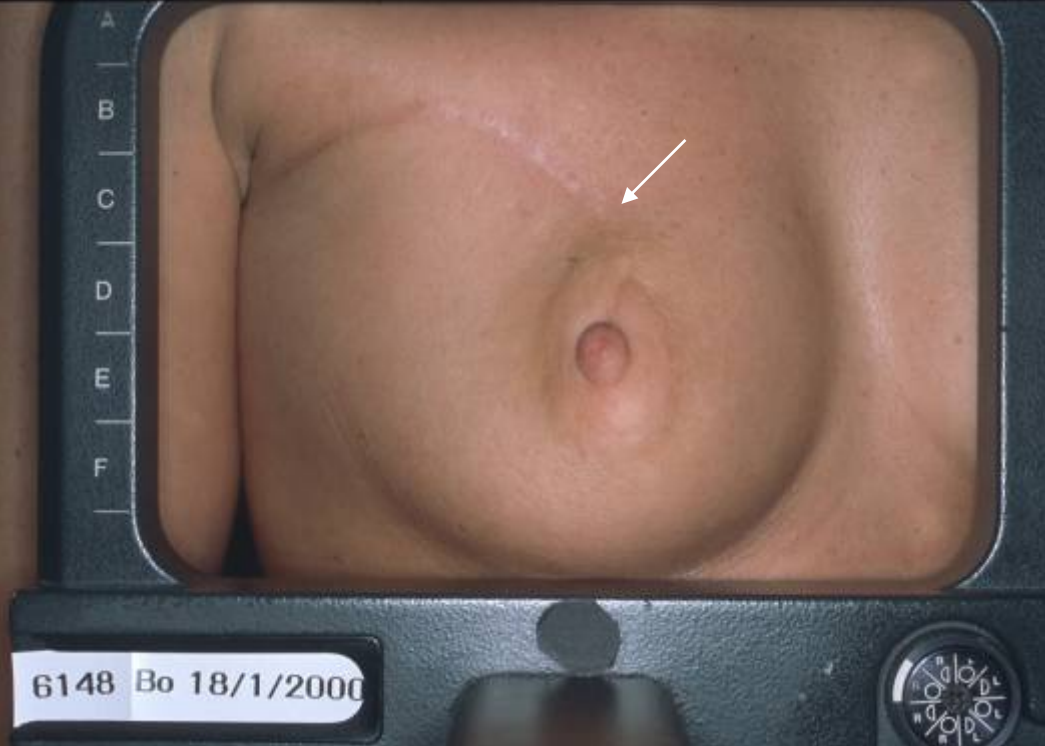
● Pz. 6128 Left Lateral Pre-op

Pt.6128 after surgery : Normal



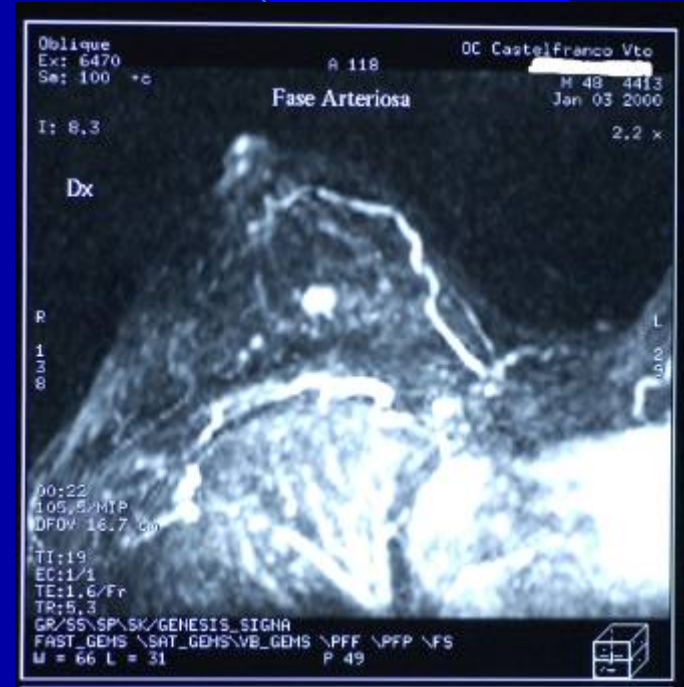
● Pz.6128 Mammography 25-10-1999

● Pz.6128 lateral left 18-10-2000



6148 correspondence between MRI and DATG

- A 40-year-old woman operated elsewhere for Ductal Infiltrating Carcinoma with radiotherapy. MRI shows a local relapse that is supported by DATG.



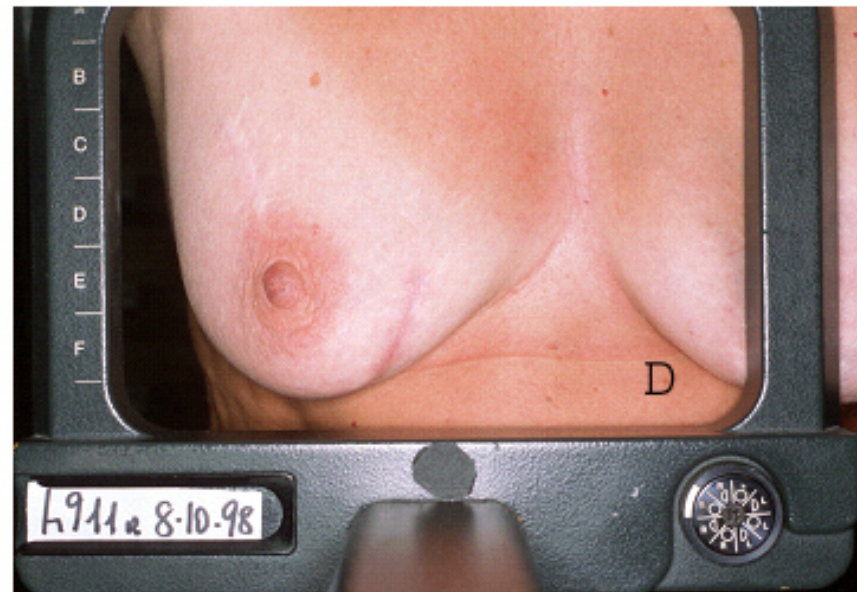
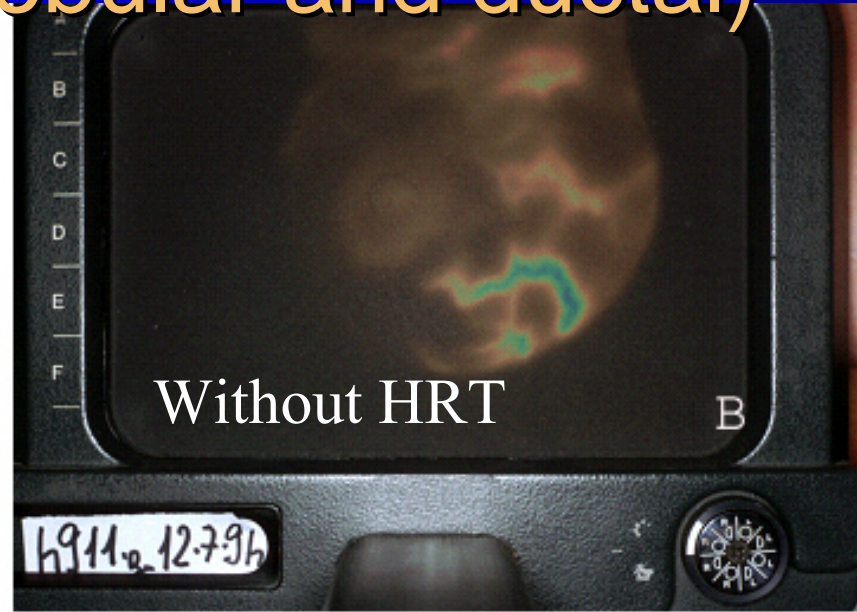
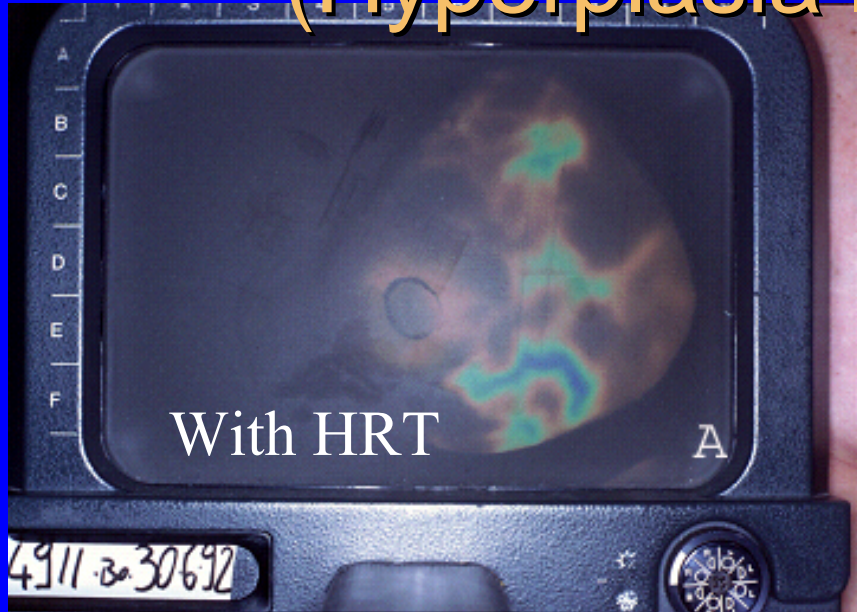
DATG Applications

Hormone Replacement Therapy

604 Long follow-up with HRT



Long follow-up with HRT and biopsy (Hyperplasia lobular and ductal)



Genetics



4779

BRCA1



4779 after surgery:
“Atypical lobular Hyperplasia”



Young Patient

17 year old: “papillary duct hyperplasia of the breast”

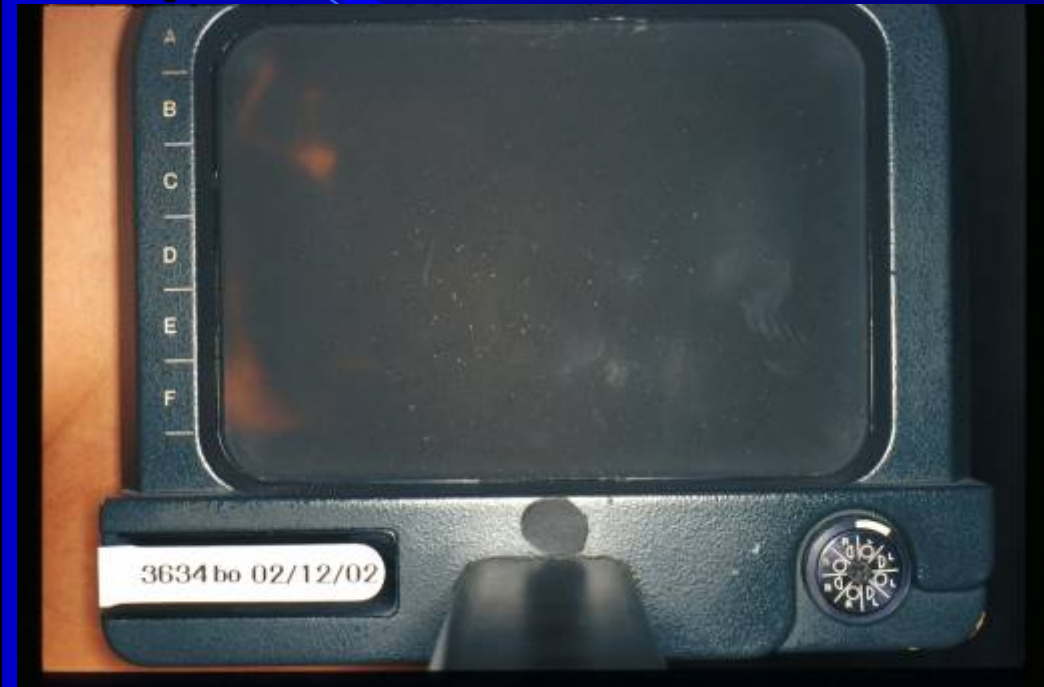


17 year old: “papillary duct hyperplasia of the breast”

-post. op-

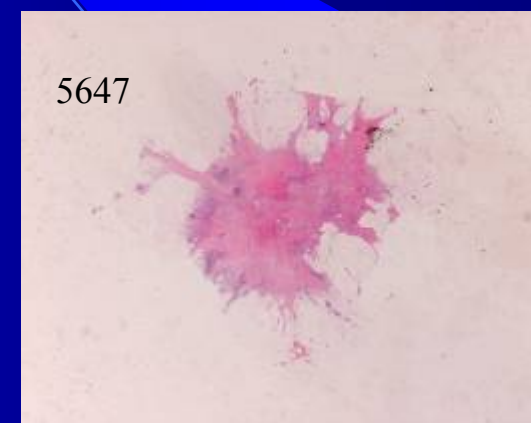
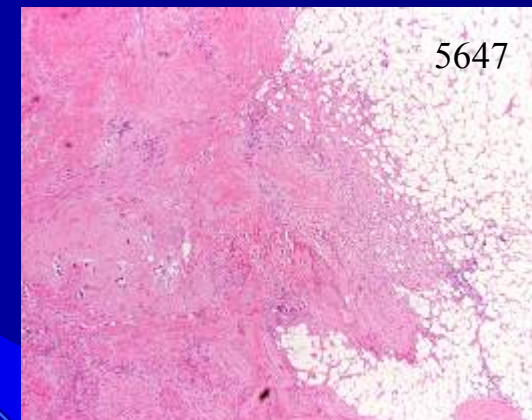
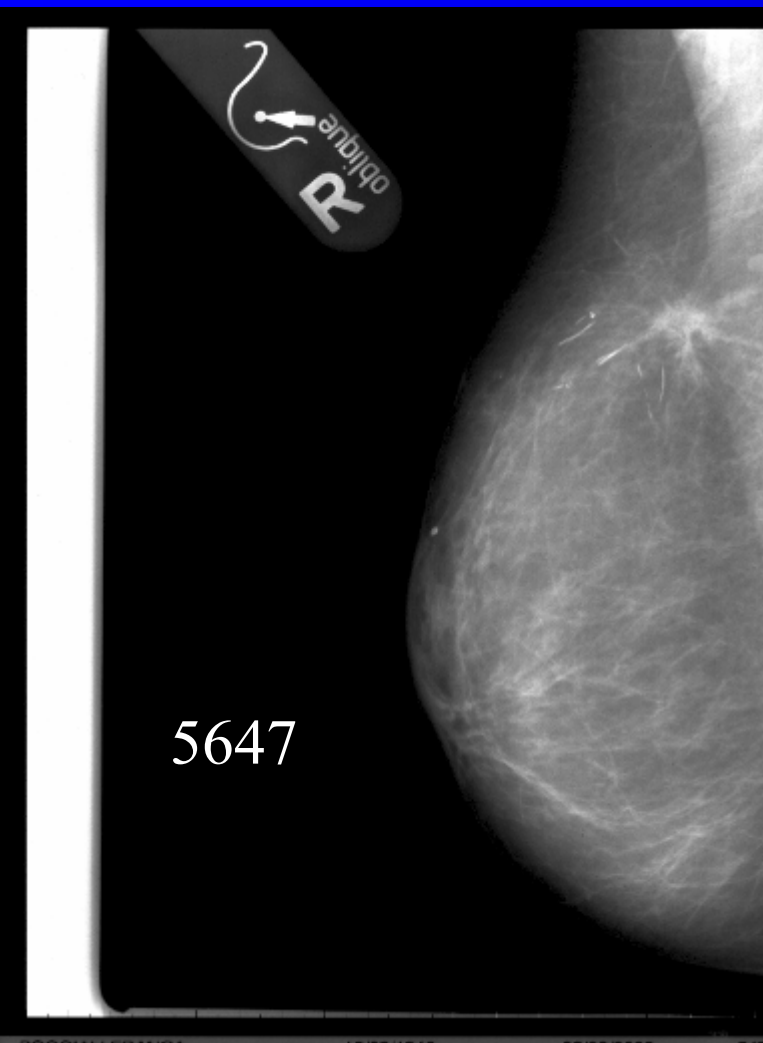


3634-front left 23-6-87
Pre-op.



3634-front left 2-12-02
Post-op.

Integrated Diagnosis



34 year old patient
Hormonal stimulation for infertility



3N+/15

A: Ductal Infiltrating
Carcinoma
G3

Controlateral is normal

B: Ductal Infiltrating
Carcinoma
with intraductal
G2

Patient with fine needle aspiration (elsewhere)
positive for infiltrating ductal carcinoma. **A**
The DATG shows a second neoplastic localization
B

Screening

DATG pattern remains the same over 16 years (in absence of pathology)



● 1041 15-3-79



● 1041 9-11-95

● **DATG is useful for screening**

Twenty-year follow up

● Screening



- Twenty-year follow up with no sign of pathology.
- Note that the DATG pattern remained unchanged throughout this period, with a slight decline in flow lines because of the onset of menopause.

DATG pattern remains the same over 25 years (in absence of pathology)



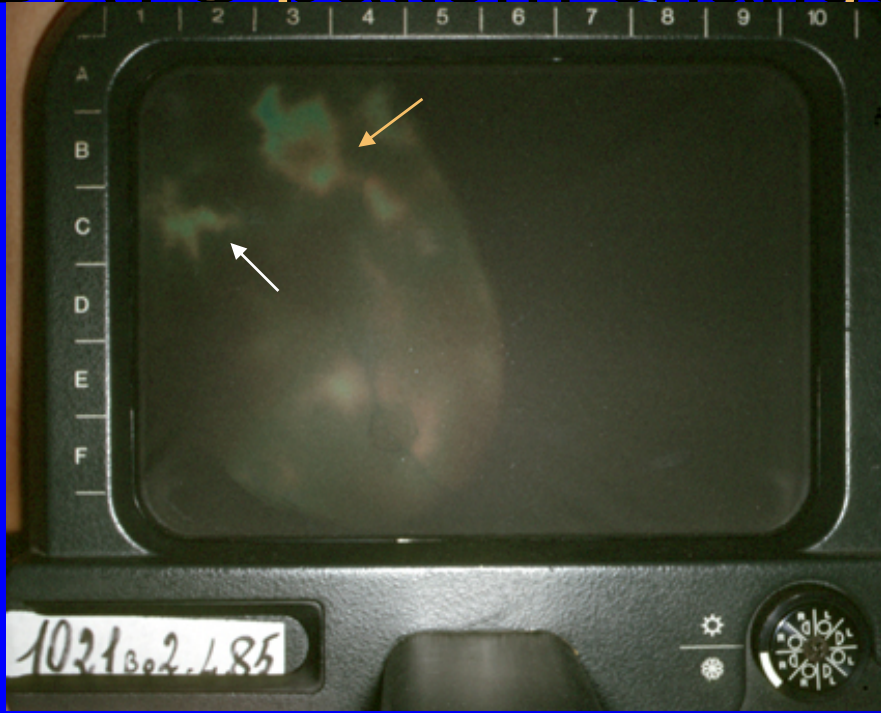
657 Lateral dx 14-3-78



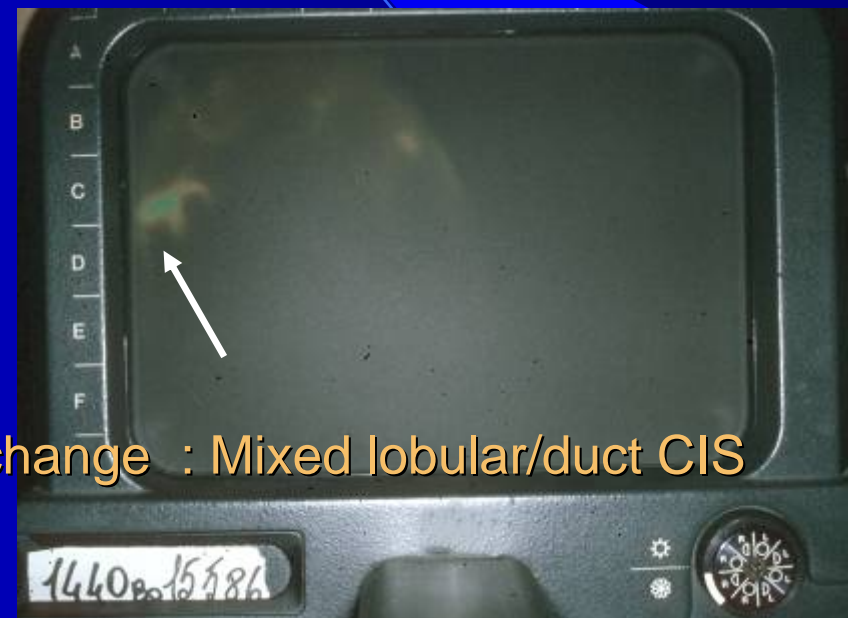
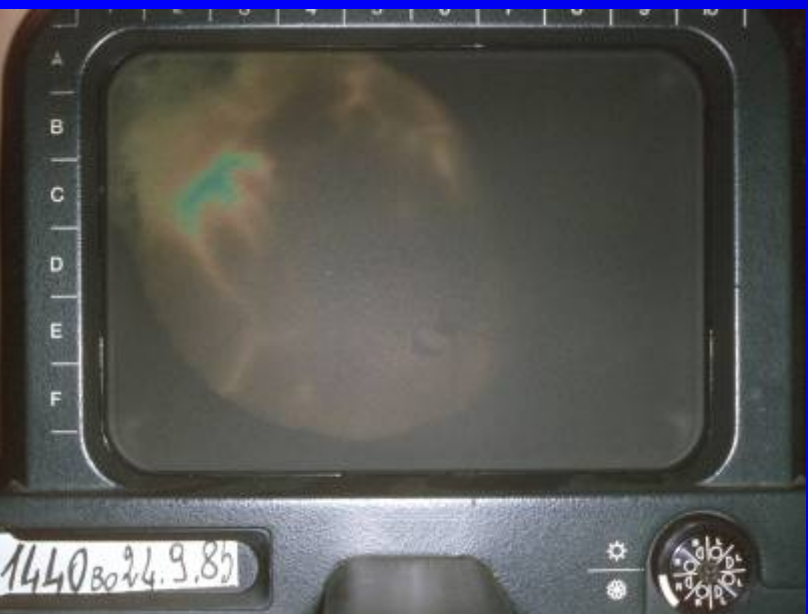
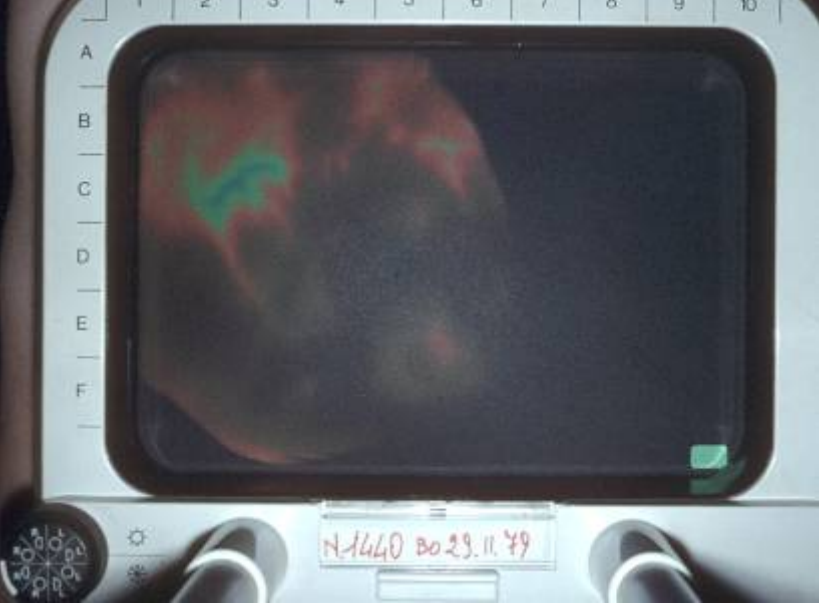
657 Lateral dx 27-11-03

- **DATG is useful for screening**

DATG pattern changes in presence of pathology

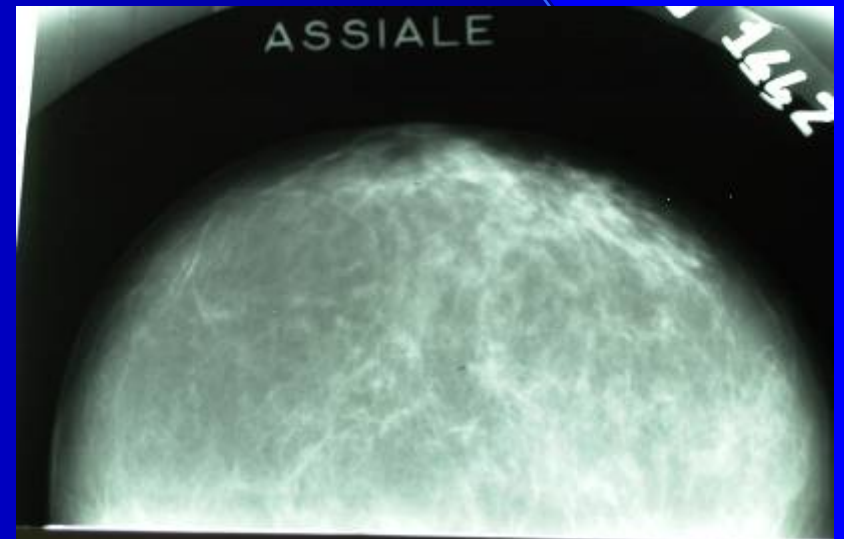


- The two flow-lines (white arrow) of the external mammary are initially normal
- 15 months later one remains the same and the other disappears to form a new line with the acromial. (red arrow) Both go on to feed a lobular in situ carcinoma (1 mm. in diameter)
- This new flowlines (12-15 cm. long) feed such very small tumor.

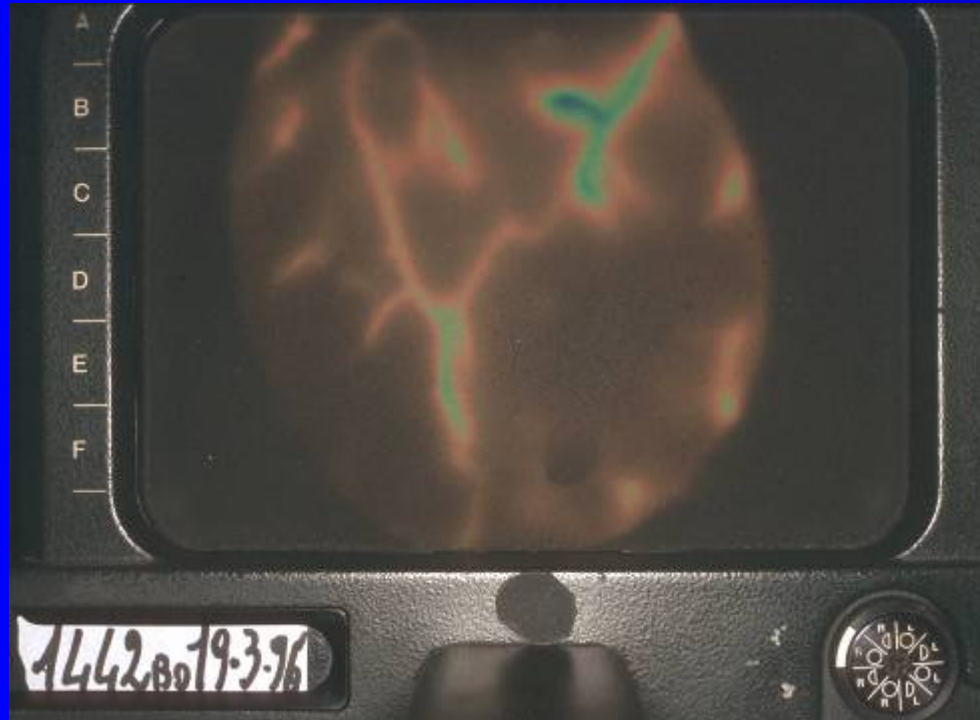


Dramatic change : Mixed lobular/duct CIS

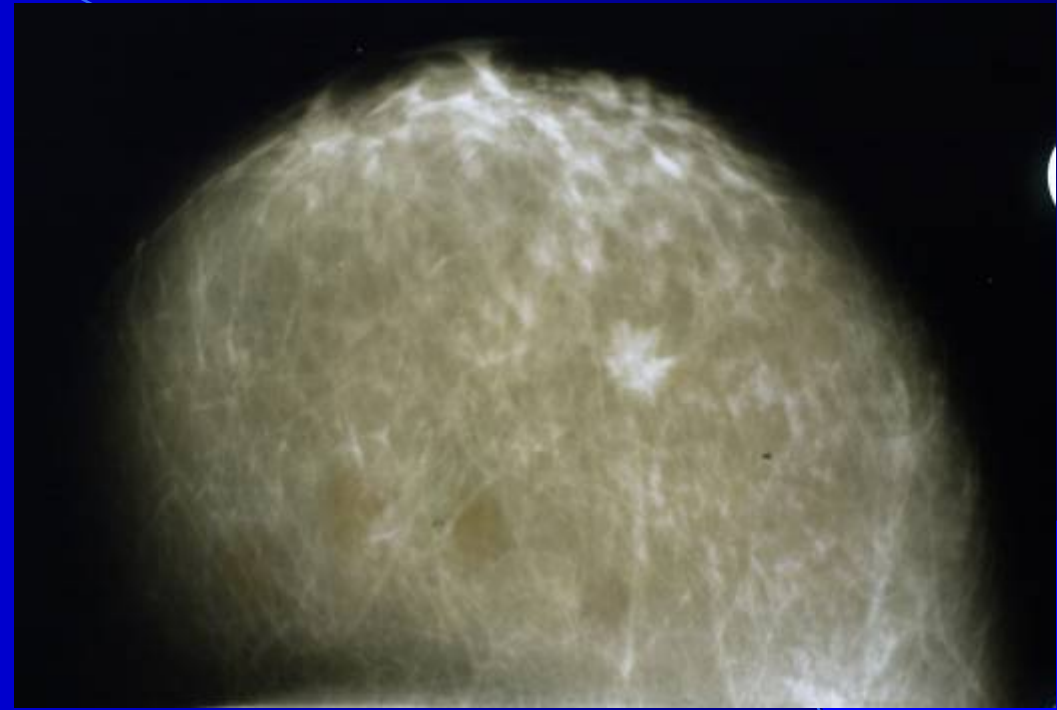
18 years earlier...



● Xray Mammography: 17-3-1994



- DATG: 19-3-96



- X-Ray Mammography: 15-3-96



After surgery

Latest references

2003-6

Naccarato AG, Viacava P, Vignati S, Fanelli G, Bonadio AG, Montruccoli G, Bevilacqua G.
Bio-morphological events in the development of the human female mammary gland
from fetal age to puberty.
VIRCHOWS ARCHIV-AN INTERNATIONAL JOURNAL OF PATHOLOGY,
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Bevilacqua G,*
Definition of the microvascular pattern of the normal human adult mammary gland.,
JOURNAL OF ANATOMY,
vol. 203, pp. 599-603, 2003

G.C. Montruccoli, D. Montruccoli Salmi, F. Casali
A new type of breast contact thermography plate: a preliminary and qualitative investigation of its potentiality on phantoms.
PHYSICA MEDICA
Vol. XX, N.1, January-March 2004 pp.27-31

*Daniele Montruccoli , Franco Casali , Stefano Brusori, Paolo Barillari,
Corrado Scipioni et Gian Carlo Montruccoli*
“L’angiothermographie dynamique : un avenir ?”
L’AGENDA GYNECOLOGIE , **Mars 2005 pag.42-43**

G.C. Montruccoli, D. Montruccoli, D. Barnabe’, V. Altomare
Thermography fiction or reality?
INTERNATIONAL JOURNAL OF OBSTETRICS AND GYNAECOLOGY
Vol. 83 Supplement N.3 pag.18 November 2-7 2003

*G. C. Montruccoli, D. Montruccoli, F. Casali, S. Brusori, W. F. Grigioni, A. G.
Naccarato, P. Viacava, N. Decarli, A. Cavazzana, G. Bevilacqua.*
Clinical application of a new thermographic plate: histopathological findings of 1027 breast lesions.
95TH AMERICAN ASSOCIATION FOR CANCER RESEARCH
AACR ANNUAL MEETING 27-31 MARCH 2004

*Viacava P., Naccarato A.G., Bocci G., Fanelli G., Aretini P., Lonobile A.,
Montruccoli G.C., Bevilacqua G.*
Angiogenesis and VEGF expression in pre-invasive lesions of human breast .
JOURNAL OF PATHOLOGY
2004; 204: 140-146

COLLABORATIVE GROUPS IN DATG CLINICAL AND RESEARCH

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- *G.Lindeque*
University of Pretoria-South Africa
- *D.Vanel*
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- *F.Schmitt-M.J.Cardoso*
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Centro prevenzione mammaria e terapia – Avezzano-Italy
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- *J.Bojages*
National Breast cancer center –Sydney
- *V.Altomare*
University Campus Biomedico -Rome
- *D.Montrucoli*
University of Rome La Sapienza-Italy

MONTRUCCOLI PROJECT

Objectives

- Study of breast carcinogenesis by molecular biology, proteomics and genomics
- Research and development of dynamic angiothermography for screening and diagnosis of early breast cancer



International clinical protocol coordinated by
Geneva Foundation for Medical Education and Research
&
World Health Organization (WHO).
Department of Reproductive Health and Research

- Double –blind prospective study comparing DATG, US, X-Ray and MRI.
- Sensitivity & specificity of DATG / X-Ray against Histology as “gold standard”- Screening
- DATG sensitivity to young BRCA 1&2 carriers

Partners:

Scientific:

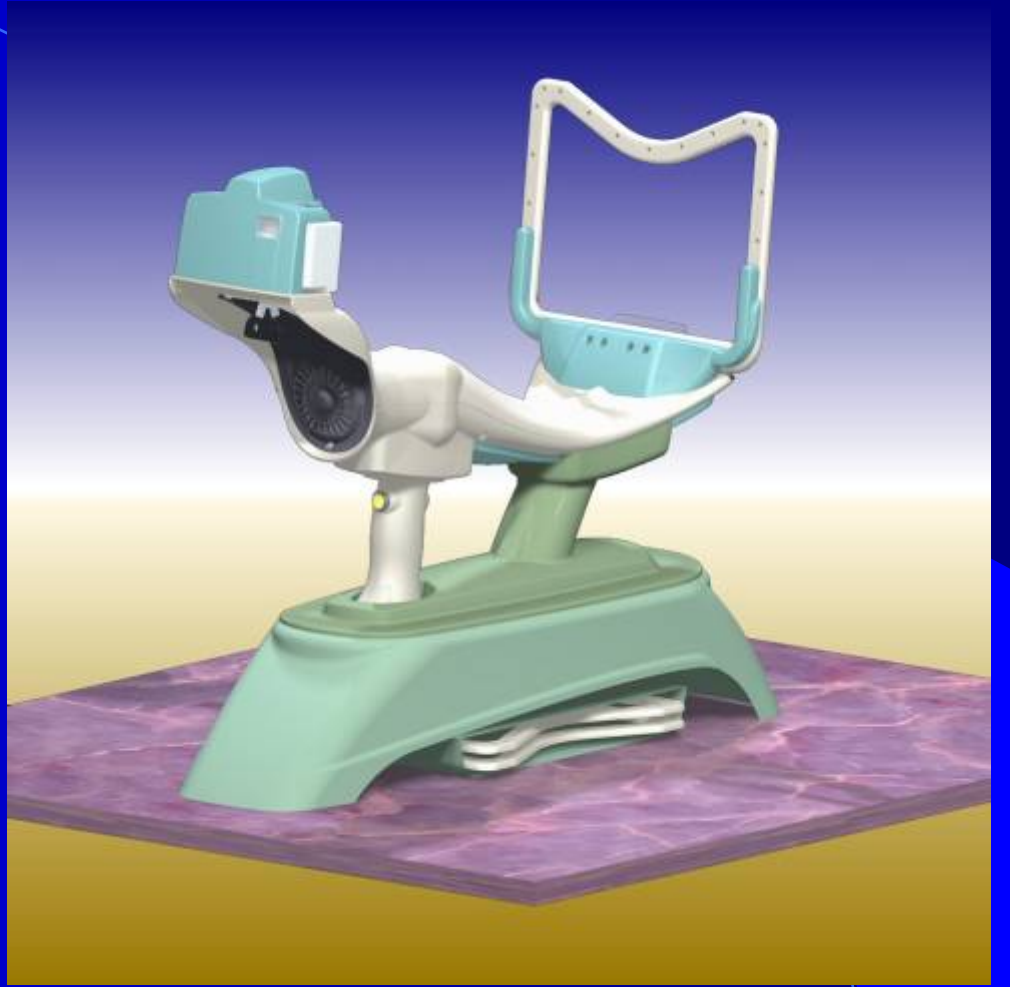
● F.I.G.O.

● S.I.S.

● G.F.M.E.R.-WHO



EQUIPMENT



DATG: practical considerations

- DATG is:
 - *Rapid*
 - *Economical*: (limited equipment and maintenance costs)
 - *Completely non-invasive*
- Can be used *at any age*
- *Very good compliance*
- *Breast cancer prevention (even detection of lobular neoplasia)*
- No radiations, No chemical, No pain
- Repetitive and Reproducible
- Rapid performance time, immediate response



www.datg.org

The DATG clinical protocol initiative is an international effort under the aegis of GFMER.

Please address your queries to

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or visit

www.datg.org

Prof. Gian Carlo Montruccoli



F.I.G.O. Oncological Committee
S.I.S. Expert Member

Thank You