Dynamic angiothermography

A new technology for breast cancer screening and diagnosis

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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 method based on the measurement of thermal gradients ($\Delta T$) evaluated by image coloration

Qualitative method based on the detailed patterns of functional blood flows

Old Contact Thermography
- Quantitative method
- based on the measurement of thermal gradients ($\Delta T$) evaluated by image coloration

Dynamic Angiothermography - DATG
- Qualitative method
- based on the detailed patterns of functional blood flows
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.

From: “A new type of breast contact thermography plate: a preliminary and qualitative investigation of its potentiality on phantoms”
Physica Medica  (Vol. XX, N. 1January-March 2004 pp.27-31)
TEST 1

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

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)
University of Bologna’s Department of Physics

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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)
Scheme of vascular anatomy of left breast

Cutaneous projection of the breast’s main arteries.

Fig. 5. — Arteries drawn according to their cutaneous projection on the normal breast.
First you cool the skin to remove any background noise
Normal 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.
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.
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.
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 Hyperplasia
In situ Cancer
Progression of angiogenesis
Hyperplasia
Invasive cancer
DATG
## 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.

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

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

With HRT

Without HRT

After surgery
Genetics
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”

-pre-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

A: Ductal Infiltrating Carcinoma
   G3

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

Controlateral is normal

3N+/15
Screening
DATG pattern remains the same over 16 years (in absence of pathology)

* DATG is useful for screening

- 1041 15-3-79
- 1041 9-11-95
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
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...
X-ray mammography: 17-3-1994
- DATG: 19-3-96
- X-Ray Mammography: 15-3-96
After surgery
Bio-morphological events in the development of the human female mammary gland from fetal age to puberty.

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

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,
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Thermography fiction or reality?
INTERNATIONAL JOURNAL OF OBSTETRICS AND GYNAECOLOGY Vol. 83 Supplement N.3 pag.18 November 2-7 2003

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Clinical application of a new thermographic plate: histophathological 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.,
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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

- **A. Campana**
  Geneva Foundation for Medical Education and Research

- **M. Merialdi**
  World Health Organization. Department of Reproductive Health and Research.

- **J.A. Pinotti; M. Pinotti; F. Carvalho**
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- **G. Lindeque**
  University of Pretoria-South Africa

- **D. Vanel**
  Institut Gustave Roussy-Villejuif- France

- **F. Schmitt-M. J. Cardoso**
  University of Porto-Portugal

- **G. Bevilacqua; A. Cavazzana**
  University of Pisa-Italy

- **C. Scipioni**
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- **J. Bojages**
  National Breast cancer center – Sydney

- **V. Altomare**
  University Campus Biomedico -Rome

- **D. Montruccoli**
  University of Rome La Sapienza-Italy

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

Please address your queries to daniele@montruccoli.it or visit www.datg.org
Prof. Gian Carlo Montruccoli

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

Thank You