SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Unità Sanitaria Locale di Reggio Emilia
IRCCS Istituto in tecnologie avanzate e modelli assistenziali in oncologia

# Stato dell'arte sull'uso della tomosintesi (DBT) nel programma di screening mammografico ed esperienze regionali.

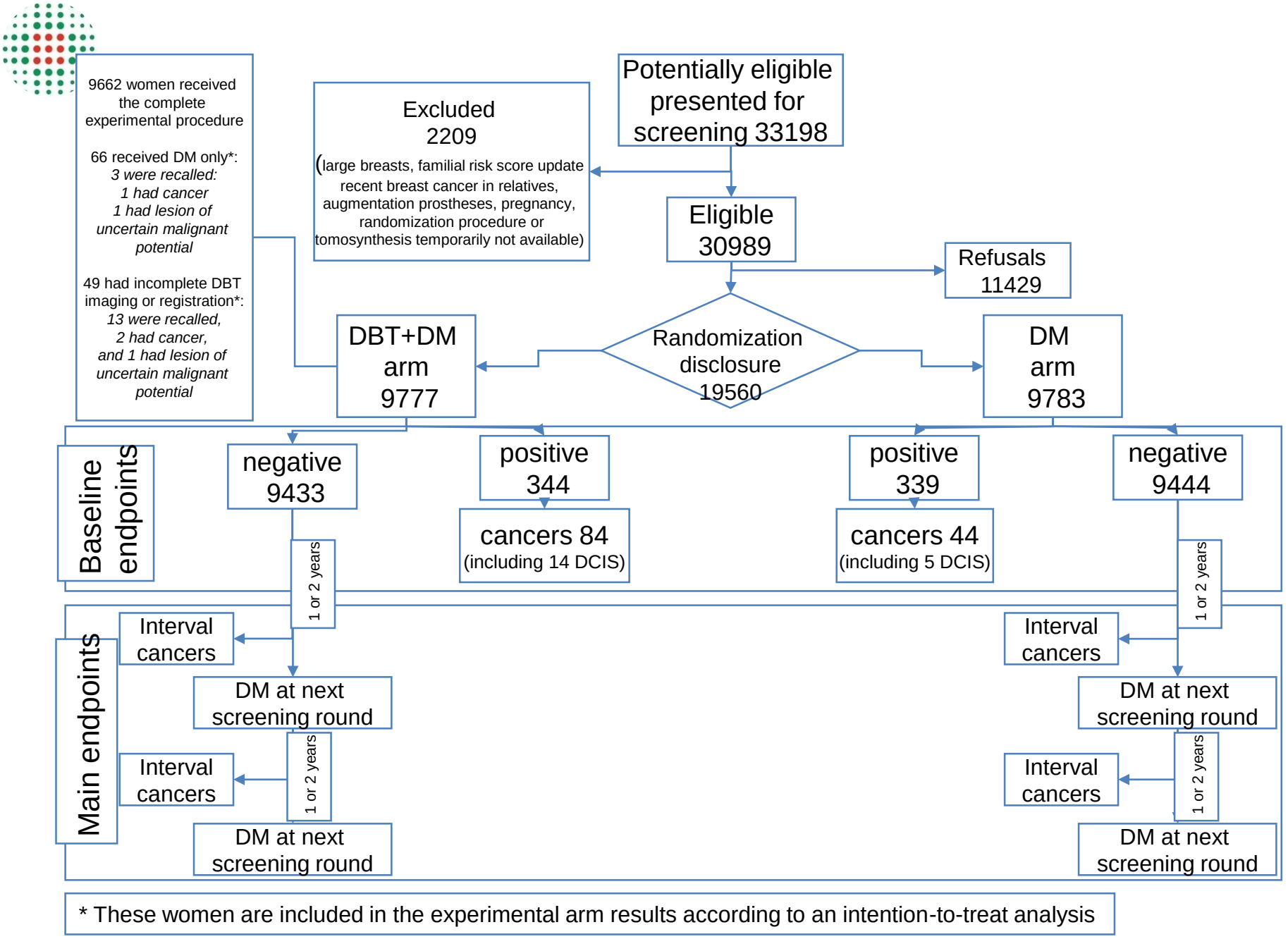
**Dott.ssa Rita VACONDIO**

*Bologna, 8 Marzo 2018*

# L’esperienza di Reggio Emilia :

- Reggio Emilia Tomosynthesis trial (RETomo)

  Marzo 2014 –Luglio 2017


9662 women received the complete experimental procedure
66 received DM only*:
3 were recalled:
1 had cancer
1 had lesion of uncertain malignant potential
49 had incomplete DBT imaging or registration*:
13 were recalled,
2 had cancer,
and 1 had lesion of uncertain malignant potential
Excluded 2209
(large breasts, familial risk score update recent breast cancer in relatives, augmentation prostheses, pregnancy, randomization procedure or tomosynthesis temporarily not available)
Potentially eligible presented for screening 33198
Eligible 30989
Refusals 11429
Randomization disclosure 19560
DBT+DM arm 9777
DM arm 9783
Baseline endpoints
negative 9433
positive 344
cancers 84 (including 14 DCIS)
positive 339
cancers 44 (including 5 DCIS)
negative 9444
1 or 2 years
1 or 2 years
Main endpoints
Interval cancers
DM at next screening round
Interval cancers
1 or 2 years
DM at next screening round
Interval cancers
DM at next screening round
Interval cancers
1 or 2 years
DM at next screening round
* These women are included in the experimental arm results according to an intention-to-treat analysis

# RE Tomo Trial

| | Braccio CONTROLLO | | | Braccio STUDIO | | |
|---|---|---|---|---|---|---|
| *II Interim Analysis* *March 2016* | FFDM 45-49 y/o | FFDM 50-59 y/o | FFDM 60-70 y/o | DBT + FFDM 45-49 y/o | DBT + FFDM 50-59 y/o | DBT + FFDM 60-70 y/o |
| ***Recall Rate*** | 3.7 % | 3.5 % | 3.3 % | 3.9 % | 3.2 % | 3.7 % |
| | **3.5 %** | | | **3.5 %** | | |
| ***VPP*** | 7.8 % | 12.8 % | 17.6 % | 13.4 % | 28.5 % | 29.1 % |
| | **13.0 %** | | | **24.1%** | | |
| ***Detection Rate*** | 2.9 ‰ | 4.4 ‰ | 5.8 ‰ | 5.2 ‰ | 9.0 ‰ | 10.5 ‰ |
| | **4.5 ‰** | | | **8.6 ‰** | | |

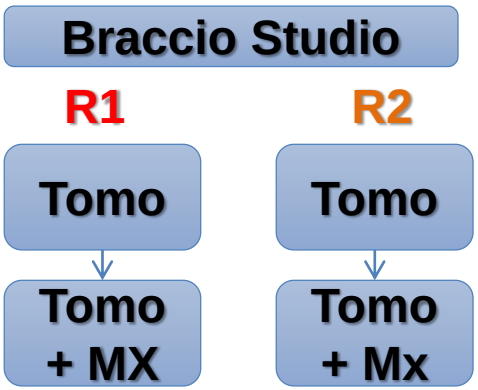
**+90%**

**vantaggio di detection rate è presente in tutte le fasce d' età e in tutte le densità**

# BIRADS DENSITY

| | DBT+DM (experim arm) | DM |
|---|---|---|
| A | 4 | 2 |
| B | 25 | 12 |
| C | 27 | 18 |
| D | 16 | 7 |
| N.A. | 11 | 5 |

# RE Tomo Trial – *Detection Rate*




*Solo studio*

*Decisione!*

| Study Arm | *Recall* | *Positive* | Visibili SOLO in TOMO |
|---|---|---|---|
| 9777 | 344 | 83 | 20 (/83) = **24%** |

# RE Tomo Trial – *Detection Rate*

| Study Arm | *Recall* | *Positive* | Visibili solo in TOMO |
|---|---|---|---|
| **9777** | **344** | **83** | **20** (/83) = **24%** |

| Hystology | In situ | Invasive |
|---|---|---|
| | 1 | 19 |
| Ductal | 1 | 13 |
| Lobular | | 5 |
| Medullary | | 1 |

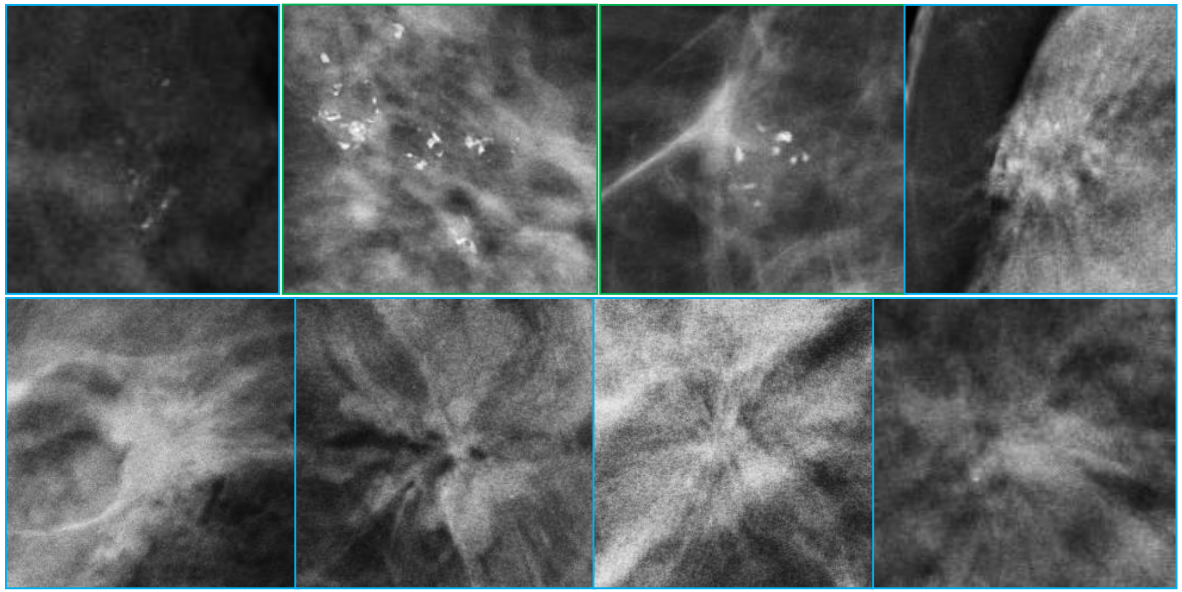
| Grade | G1 | G2 |
|---|---|---|
| | 4 | 13 |

| Br. Density | |
|---|---|
| A | 0 |
| B | 4 |
| C | 9 |
| D | 7 |

| Path Size | ∅ < 10 mm | 10 mm ≤ ∅< 20 mm |
|---|---|---|
| | 1 | 19 |

# B3 & Lesioni ad alto rischio

| *High-Risk Lesion* | Braccio Controllo | Braccio Studio |
|---|---|---|
| **B3** | 2 | 8 |
| **Lobular Ca in situ** | 1 | 0 |



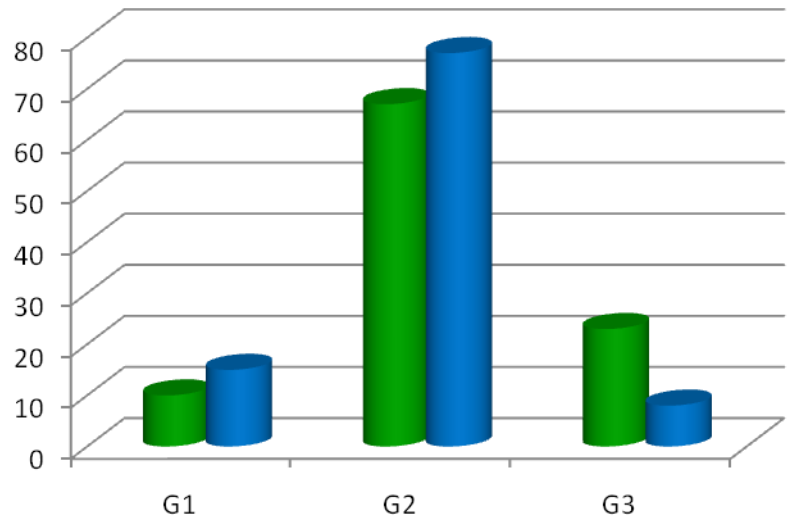
| *B3* | Final Diagnosis on Surgical Specimen |
|---|---|
| **Pz 1** | Flat Epithelial Atypia |
| **Pz 2** | Lobular Ca in situ |
| **Pz 3** | Radial Scar + ADH |
| **Pz 4** | Mucocele + ADH |
| **Pz 5** | Radial Scar + ADH |
| **Pz 6** | Radial Scar + ADH |
| **Pz 7** | Radial Scar |
| **Pz 8** | Papilloma |
| **Pz 9** | Radial Scar |
| **Pz 10** | Radial Scar |
| **Pz 11** | Radial Scar |

| | EXPERIMENTAL ARM BDT+DM | CONTROL ARM DM |
|---|---|---|
| **DIMENSION LESION** | | |
| <10 mm | 31 | 16 |
| >=10<20 mm | 31 | 14 |
| >=20 mm | 7 | 8 |
| N.A. | 0 | 1 |
| **ESTROGEN RECEPTOR** | | |
| >=10% | 75 | 40 |
| <10% | 5 | 3 |
| N.A. | 3 | 1 |
| **PROGESTERONE RECEPTOR** | | |
| >=10% | 62 | 26 |
| <10% | 18 | 17 |
| N.A. | 3 | 1 |
| **HER2** | | |
| Positive | 6 | 11 |
| Negative | 58 | 28 |
| N.A. | 19 | 5 |
| **Ki67** | | |
| Positive(>=20%) | 17 | 11 |
| Negative (<20%) | 50 | 27 |
| N.A. | 16 | 6 |
| **TRIPLE NEGATIVE** | 0 | 2 |

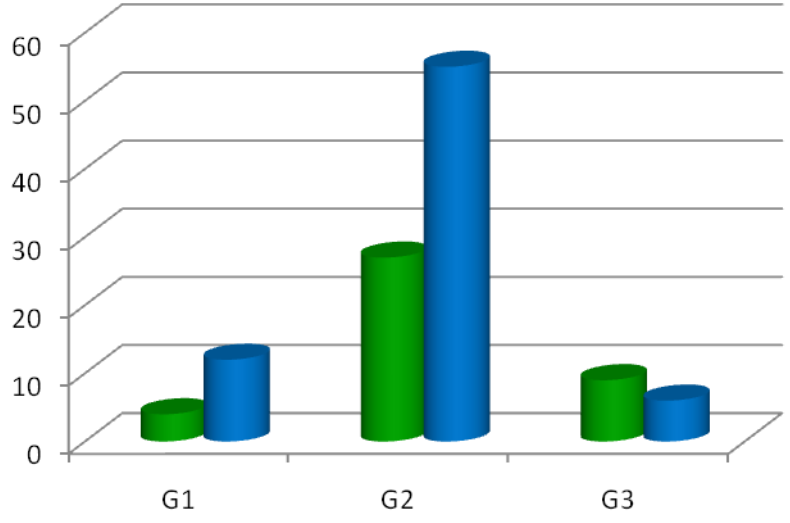
# RE Tomo Trial - Grado

| *Grado* | Br. Controllo MX | Br. Studio TOMO + MX |
|---|---|---|
| G1 | 10 % | 15 % |
| G2 | 67 % | 77 % |
| G3 | 23 % | 8 % |

**Percentuale**




**Numero di Pazenti**



# RE Tomo Trial - Tempi Lettura

| | 1st Lettore | 2nd Lettore | RICHIAMO | |
|---|---|---|---|---|
| | | | 1st Lettore | 2nd Lettore |
| FFDM | 37 s | 32 s | 99 s | 93 s |
| DBT + FFDM | 60 s | 56 s | 108 s | 108 s |
| Δ % | + 62 % | + 75 % | + 9 % | + 16 % |
| p value | < 0.05 | < 0.05 | > 0.05 | > 0.05 |

In caso di richiami l'incremento del tempo di lettura non è significativo, suggerendo che tale aumento sia correlato al maggior numero di immagini stesso della TOMO piuttosto che alla loro interpretazione

| Trial/studio | MX | MX + Tomo | Δ % |
|---|---|---|---|
| ***Trento**** | 33 s | 77 s | ***+ 135 %*** |
| ***Oslo***** | 48 s | 89 s | ***+ 85 %*** |
| ***Boston***** | 114 s | 168 s | ***+ 47 %*** |

Bernardi D, Ciatto S et al:BJR,2012 **Skaane P et al.:Eur Radiol.2013 ***Dang PA et al: Radiology,2014

# Tempi & Risorse

TOMO
*Aumenta tempi di lettura*

Screening
Lettura

Screening
ASSESSMENT
dei richiami

TOMO
*Aumenta VPP*
*riducendo i FP e gli assessment non necessari*

Percorso
Terapeutico
(chirurgia / chemiotp)

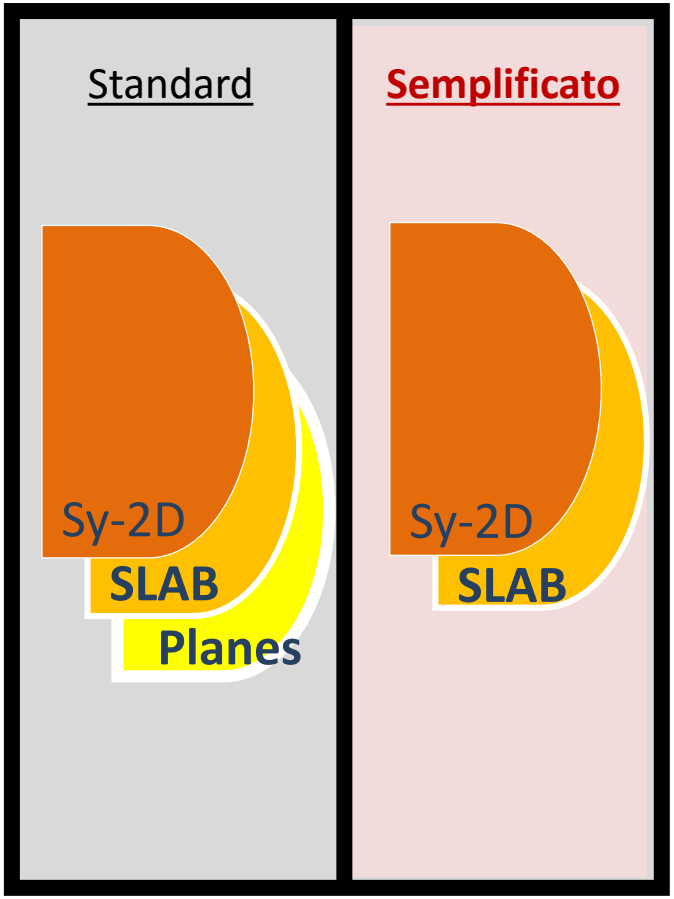
TOMO
*Diagnosi di «Early invasive cancers»: riduce impatto terapeutico??*

# RE Tomo Visualization Protocols Study

PROTOCOLLO SEMPLIFICATO: riducendo il numero di immagini analizzate si presuppone di ridurre il tempo di lettura

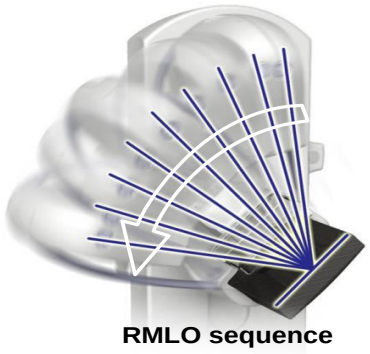
| **N. of images in a "medium" breast** (5 cm thickness) x Projection |
|---|
| 1 |
| 5 |
| 50 |

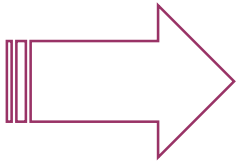
| Standard | **Semplificato** |
|---|---|
| Sy-2D | **Sy-2D** |
| SLAB | **SLAB** |
| Planes | |
| **56** images | **6** images |

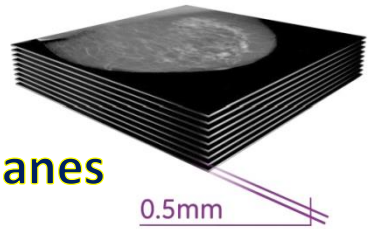


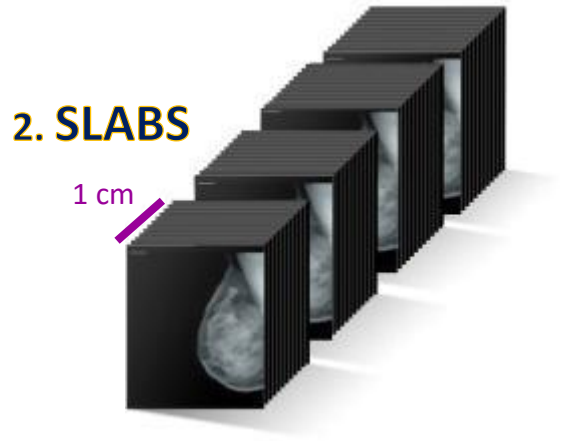
# Tomosintesi

Per ogni proiezione TOMO
i dati grezzi permettono
diverse ricostruzioni

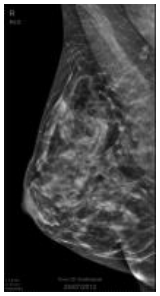





3. Synthetic-2D
(Sy-2D)



# RE Tomo Visualization Protocols Study

Valutazione retrospettiva di 2 set di Tomo prese dal Braccio di Studio

**Double Independent Reading**

Tutte le Tomo sono state lette da 2 radiologi con entrambi I protocolli Standar e Semplificato, dopo 3 mesi di wash out


**1st SET**: per valutare la **specificità**

| 1st Set | Tomo | Positive |
|---|---|---|
| *Pazienti* | *894* | *12* |
| Letture | 1788 | **24** |

**2nd SET**: arricchito per valutare la **sensibilità**

| 2nd Set | Tomo | Positive |
|---|---|---|
| Letture | 546 | **40** |

# RE Tomo Visualization Protocols Study

| *median reading time* | Standard Protocol | **Simplified Protocol** |
|---|---|---|
| ***Lettore 1*** | 60 s | 35 s |
| ***Lettore 2*** | 71 s | 55 s |
| ***Lettore 3*** | 97 s | 69 s |

Riduzione di circa il 20%-30% del tempo di lettura medio per tutti i lettori

# RE Tomo Visualization Protocols Study

## 1st SET: to estimate specificity

| 1st Set | DBT | Negative | Positive |
|---|---|---|---|
| Patients | *894* | *882* | *12* |
| Readings | 1788 | 1764 | 24 |

| | Standard Protocol | Simplified Protocol |
|---|---|---|
| VN | 1699/ 1764 | **1727 / 1764** |
| ***Specificità*** | *96.3 %* | ***97.9%*** |

*p=0.005*

| | | |
|---|---|---|
| **Inter-reader agreement** | *0.57* | ***0.70*** |

# RE Tomo Visualization Protocols Study

## to estimate **sensitivity**

| 2° + 1° Set | Positive | Positive | considering all the independent readings obtained in the two sets |
|---|---|---|---|
| Readings | 40 | 24 | **64** |

| | Standard Protocol | **Simplified Protocol** |
|---|---|---|
| TP readings | **58/64** | 53/ 64 |
| ***Sensitivity*** | ***90.6 %*** | ***82.8 %*** |
| | | *p=0.19* |

with the Simplified Protocol, 4 cases were missed by both readers…

# RE Tomo Visualization Protocols Study Limiti

- workstation  separate dalla pratica clinica quotidiana e non ottimizzate
- Studio retrospettivo: lettori non sottoposti alla “pressione” reale della pratica clinica
- Potenza dello studio limitata per la valutazione della sensibilità
- Curva d’apprendimento!!

| | 1° Set | 2° Set |
|---|---|---|
| *Falsi Negativi* | *5* | *0* |

# RE Tomo Visualization Protocols Study Conclusioni

- Il **protocollo semplificato** (**Sy2D + SLABS**) si è mostrato efficace nel ridurre il tempo di lettura (circa **20 %**)

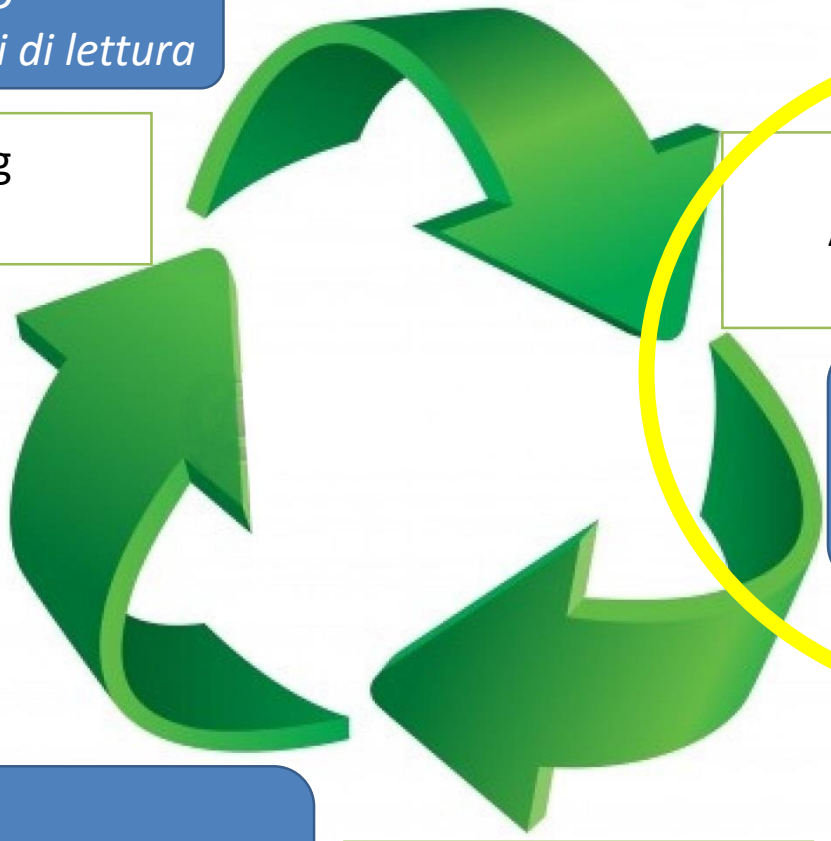
- **aumentando la specificità e riproducibilità delle letture in una popolazione di screening**

- ma con un potenziale impatto negativo sulla sensibilità

# Tempi & Risorse

TOMO
*Aumenta tempi di lettura*

Screening
Lettura



Screening
ASSESSMENT
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TOMO
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TOMO
*Diagnosi di «Early invasive cancers»: riduce impatto terapeutico??*

Percorso
Terapeutico
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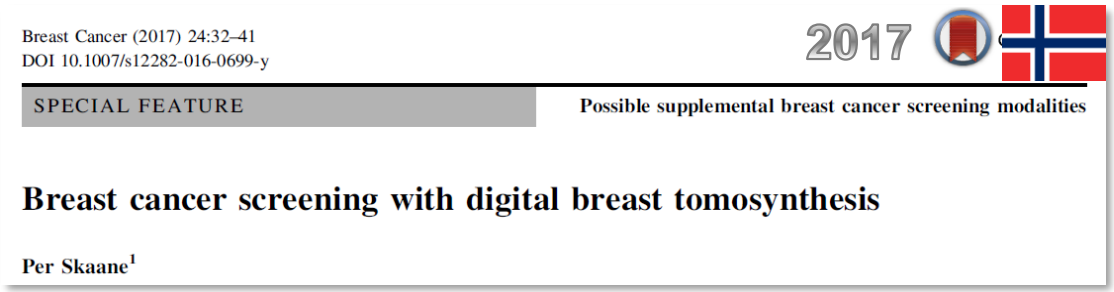
# Tomo & Screening: stato dell'arte


Breast Cancer (2017) 24:32–41
DOI 10.1007/s12282-016-0699-y

2017

SPECIAL FEATURE — Possible supplemental breast cancer screening modalities

**Breast cancer screening with digital breast tomosynthesis**

Per Skaane[1]

"The retrospective US studies and the prospective European trials on tomosynthesis in screening have confirmed the **higher sensitivity and higher specificity using DBT** as *adjunct* to 2D, as shown in the experimental clinical studies.

- The ***higher cancer conspicuity and visibility*** on DBT **increase the cancer detection rate** significantly
- The ***higher specificity*** causes a **reduction in the recall rate**

**...DBT has been considered to be the next future of breast cancer screening."**

# Tomo & Screening: stato dell'arte

- ***Studi Retrospettivi*** di screening dagli USA
- ***Significativa riduzione della RR***

| *Model-adjusted* | RR |
|---|---|
| DM | 10.7 % (95 % CI 8.9–12.4) |
| DM + DBT | 9.1 % (95 % CI 7.3–10.8) |

*statistically significant* ***decrease in the RR*** *(from 14 % to 63 %)*

- 3 trial europeo ***prospettivi*** in screening
- ***Significativo aumento della DR***

| DR | STORM *Trento/Verona* | OTST *Oslo* | MBTST *Malmø* |
|---|---|---|---|
| DM | 5.3 ‰ | 6.1 ‰ | 6.3‰ |
| DM + DBT | 8.1 ‰ | 8.0 ‰ | 8.9 ‰ |

*statistically significant* ***increase in the DR*** *(from + 27% to +53 %)*

*Skaane P, Breast Cancer (2017)*

# Tempi & Risorse

TOMO
*Aumenta tempi di lettura*

Screening
Lettura

Screening
ASSESSMENT
dei richiami

TOMO
*Aumenta VPP*
*riducendo i FP e gli assessment non necessari*

TOMO
*Diagnosi di «Early invasive cancers»: riduce impatto terapeutico??*

Percorso
Terapeutico
(chirurgia / chemiotp)

Breast Cancer Res Treat (2017) 164:557–569
DOI 10.1007/s10549-017-4298-1

REVIEW

# Benefit of adding digital breast tomosynthesis to digital mammography for breast cancer screening focused on cancer characteristics: a meta-analysis

Seong Jong Yun[1] · Chang-Woo Ryu[2] · Sun Jung Rhee[2] · Jung Kyu Ryu[2] · Ji Young Oh[2]

2017

Adding DBT to DM enabled detection of **early invasive breast cancer** that might have been missed with DM alone.

Cancers detected through DBT's addition have *a more favourable prognosis* and are *less likely to require aggressive treatment* by preventing these screening detected cancers from becoming interval or symptom-detected cancers later.

Breast Cancer Res Treat (2017) 164:557–569
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REVIEW

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STORM 2013*
Rose 2013
OTST 2013

McCarthy 2014
Greenberg 2014
Durand 2015

Lourenco 2015
MBTST 2016

STORM–2 2016*
Sharpe 2016
Powell 2017

- Pooled risk ratios showed a greater detection for **DBT + DM** than for DM alone for:
  - **invasive cancer** (1.327; 95% CI, 1.168–1.508)
  - **stage T1** (1.388; 95% CI, 1.137–1.695)
  - **nodal-negative** (1.451; 95% CI, 1.209–1.742)
  - **all histologic grades** (grade I 1.812; grade II/III 1.403)
  - **all histologic types of invasive cancer** (ductal 1.437; lobular 1.901)

However, proving that more cancers are found, even invasive cancers, is probably not sufficient to demonstrate that DBT + DM should replace conventional DM alone for breast cancer screening

- Adding DBT **did not** increase for detection of:
  - carcinoma in situ (1.198; 95% CI, 0.942–1.524)
  - stage T2 (1.391; 95% CI, 0.895–2.163)
  - nodal-positive cancer (1.336; 95% CI, 0.921–1.938)

Further evaluation should be conducted using surrogate endpoints, such as the change of the **interval cancer rate** or **progression-free survival**

Radiol med
DOI 10.1007/s11547-017-0769-z

BREAST RADIOLOGY

# Digital breast tomosynthesis (DBT): recommendations from the Italian College of Breast Radiologists (ICBR) by the Italian Society of Medical Radiology (SIRM) and the Italian Group for Mammography Screening (GISMa)

Daniela Bernardi[1] · Paolo Belli[2] · Eva Benelli[3] · Beniamino Brancato[4] · Lauro Bucchi[5] · Massimo Calabrese[6] · Luca A. Carbonaro[7] · Francesca Caumo[8] · Beatrice Cavallo-Marincola[9] · Paola Clauser[10] · Chiara Fedato[11] · Alfonso Frigerio[12] · Vania Galli[13] · Livia Giordano[14] · Paolo Giorgi Rossi[15] · Paola Golinelli[16] · Doralba Morrone[4] · Giovanna Mariscotti[17] · Laura Martincich[18] · Stefania Montemezzi[19] · Carlo Naldoni[20] · Adriana Paduos[14] · Pietro Panizza[21] · Federica Pediconi[9] · Fiammetta Querci[22] · Antonio Rizzo[23] · Gianni Saguatti[24] · Alberto Tagliafico[25] · Rubina M. Trimboli[26] · Marco Zappa[27] · Chiara Zuiani[28] · Francesco Sardanelli[7,29]

Received: 24 February 2017 / Accepted: 12 April 2017


"A generalized adoption of DBT as a first-level screening tool
should wait for a specific evidence,
in particular for a statistically significant and clinically relevant reduction
in interval cancer rate
(hopefully associated with a reduction in advanced cancer rates).»

"For high-risk women, when a mammogram is indicated, a sDM/DBT protocol should be preferred.»

Eur Radiol (2017) 27:2737–2743
DOI 10.1007/s00330-016-4612-z

BREAST

# Position paper on screening for breast cancer by the European Society of Breast Imaging (EUSOBI) and 30 national breast radiology bodies from Austria, Belgium, Bosnia and Herzegovina, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Israel, Lithuania, Moldova, The Netherlands, Norway, Poland, Portugal, Romania, Serbia, Slovakia, Spain, Sweden, Switzerland and Turkey

2017

*Reduction from 0.7 to 0.5* ***interval cancers*** *per 100 screened women with DBT*

*To avoid an increase in overdiagnosis and costs,*
*in the absence of the demonstration of cost-effectiveness of screening DBT,*
***we need evidence***
***for a statistically significant and clinically relevant reduction in the interval cancer rate***

**Randomized Clinical Trial**

# Cancri intervallo

L'incidenza dipende dal TEMPO di intervallo tra le chiamate di Screening (1 anno vs 3 anni)

Non sempre correlati a maggior gravità prognostica del k trovato

Donne che si presentano pochi giorni prima della data dello screening, dopo aver ricevuto la lettera di invito..

**Correlati a riduzione della mortalità?**

**≥ T2?**