Tomosintesi per il tumore del polmone

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Outline

• Principle of digital tomosynthesis (DTS)
• Image quality
• Dosimetry in screening
• SOS trial
  – Lung nodule analysis
• Principle of digital tomosynthesis (DTS)
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History

• The basic theoretical framework for limited angle tomography was provided in the 1930s. However, with the development of digital detectors being decades in the future, the implementation of tomosynthesis was clearly not feasible in those early days. Grant coined the term “tomosynthesis” in a landmark paper in 1972 that described the method of simple tomosynthesis reconstruction.

• Historical difficulties:
  – the residual blur from objects outside of the plane of interest
  – films (not DRs)
History

1922 Patent of Parisian A. Bocage (1892-1953)
1922 B.G. Ziedses Des Plantes (1902-1993) he then developed not only tomography but also stereoscopic techniques and subtraction techniques which became the subject of his thesis publicized in 1934.

1930 At the same time D.L. Bartelink (1894-1985) built a radiotomographic apparatus with which he made the first pictures

1930 A. Vallebona (1899-1987) from Genoa obtained his first radiotomographic image in 1930. He described two techniques. In the first one, the subject remains immobile and the system (X-ray tube–plate) pivots around an axis situated at the level of the slices

1915, by moving simultaneously the X-ray tube and the fluoroscopic screen connected by a lever, C. Baese (?) of Florence developed a radio-stereometer used during the Great War in the health formations to localize the projectiles inside a soldier’s body.
Basic geometry

a. Parallel-path motion
   • chest & abdominal
   • simpler reconstruction
   • no magnification

b. Partial isocentric motion
   • breast
   • variable magnification

c. Full isocentric motion
   • as in cone beam CT but with limited angle used in C-arm and RT
   • excellent but complex reconstruction
Reconstruction algorithm

SAA (shift and add)

• performed adequately based solely on the known positions of the x-ray tube as it travels

• overlapping blurry anatomy from outside of the plane of interest
Deblurring algorithm

MITS matrix inversion tomosynthesis

The $t_i$ plane image is the sum of the known blurring functions $f_i$ from all other planes

$$
\begin{align*}
t_1 &= s_1 \otimes f_{11} + s_2 \otimes f_{12} + \ldots + s_n \otimes f_{1n} \\
t_2 &= s_1 \otimes f_{21} + s_2 \otimes f_{22} + \ldots + s_n \otimes f_{2n} \\
&\vdots \\
t_n &= s_1 \otimes f_{n1} + s_2 \otimes f_{n2} + \ldots + s_n \otimes f_{nn}
\end{align*}
$$

in the Fourier space $s = F T^{-1} (F^{-1} T)$

- quite fast computationally
- given an object composed of a finite number of planes, can render an exact solution in the absence of noise
Deblurring algorithm

FBP filtered back projection

Usual algorithm with Hamming and Gaussian filter to control the high frequency noise amplification typical of FPB due to point spread function

- quite fast computationally
**Acquisition protocol**

<table>
<thead>
<tr>
<th>N. images</th>
<th>Oscillation angle</th>
</tr>
</thead>
<tbody>
<tr>
<td>94</td>
<td>30°</td>
</tr>
</tbody>
</table>

**PA projection**

**Rule of thumb for** $mA_{DTS} = 10 \times mA_{AEC-Xray}$

<table>
<thead>
<tr>
<th>$kV$</th>
<th>$mA$</th>
<th>msec</th>
<th>mAs</th>
<th>Execution time(sec)</th>
<th>Additional filtration</th>
</tr>
</thead>
<tbody>
<tr>
<td>120</td>
<td>125</td>
<td>2</td>
<td>0.25</td>
<td>11.4</td>
<td>Cu 0.2 mm</td>
</tr>
</tbody>
</table>
Maintaining wide latitude while preserving visualization of low-contrast features in the image is a particular challenge for chest radiography.

<table>
<thead>
<tr>
<th>( \frac{I_0}{I(10\text{cm})} )</th>
<th>( \mu ) (cm(^{-1}))</th>
<th>Tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
<td>Air</td>
</tr>
<tr>
<td>121</td>
<td>0.48</td>
<td>Bone</td>
</tr>
<tr>
<td>6</td>
<td>0.18</td>
<td>Muscle</td>
</tr>
</tbody>
</table>

\(120\text{ kV}\)
\(3\text{mmAl} + 0.2\text{ mmCu}\)

Some images....
• Principle of digital tomosynthesis (DTS)
• Image quality
• Dosimetry in screening
• SOS trial
  – Lung nodule analysis
Flat-Panel Digital Detector

Fixed Detector Specifications
Detector Size 41 cm x 41 cm
Active Matrix 2022 x 2022 pixels
Image Depth 14 Bit
Pixel Pitch 200 microns
Typical Dynamic Range 0.6 uR – 9 mR @ RQA5
Typical DQE 77% @ 0 lp @ RQA5

a single panel (non-tiled) amorphous silicon detector with a Cesium Iodide scintillator.
Image Quality

- Image Quality Phantom
- mAs adjusted to have the same dose on standard patient
- Quality indexes:
  - MTF
  - Low contrast resolution
Considering that radiological relevant nodules are larger than 5 mm, this could explain from a technical point of view, the good clinical performance of DTS.
• Principle of digital tomosynthesis (DTS)
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<table>
<thead>
<tr>
<th>CT</th>
<th>X-rays</th>
<th>DTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>kVp</td>
<td>Exp time (sec)</td>
<td>Average mA</td>
</tr>
<tr>
<td>120</td>
<td>0.4</td>
<td>300</td>
</tr>
</tbody>
</table>
Tomosynthesis dose estimation

Mean effective dose was estimated on a cohort of 20 patients using Monte Carlo software PCXMC (STUK, Helsinki, Finland)

TLD measurement were carried out in Alderson Rando anthropomorphic phantom
Mean effective dose was estimated on a cohort of 20 patients using Monte Carlo software CTexpo before and after optimization

$$E = 11.6 \pm 13.0 \text{ mSv}$$  
$$E = 4.9 \pm 1.9 \text{ mSv}$$

N.B. The CT is used in SOS to assess tomosynthesis results hence CT scan is not a screening scan.
## Results

### Dose in RX and Volume RAD exams with 0.2 mm Cu

<table>
<thead>
<tr>
<th></th>
<th>ESD [mGy]</th>
<th>E [mSv]</th>
<th>Monte Carlo</th>
<th>TLD</th>
<th>Literature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consolle</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ionization chamber</td>
<td>0.102 0.003</td>
<td>0.113 0.011</td>
<td>0.009 0.004</td>
<td>0.009 0.001</td>
<td>0.011</td>
</tr>
<tr>
<td>TLD</td>
<td>0.009</td>
<td>0.004</td>
<td>0.009 0.001</td>
<td>0.009 0.011</td>
<td>0.011</td>
</tr>
<tr>
<td>X-rays</td>
<td>0.106</td>
<td>0.066</td>
<td>0.113 0.011</td>
<td>0.009 0.004</td>
<td>0.009 0.001</td>
</tr>
<tr>
<td>DTS</td>
<td>0.994</td>
<td>0.654</td>
<td>0.954 0.095</td>
<td>0.093 0.037</td>
<td>0.089 0.009</td>
</tr>
</tbody>
</table>

### Dose in RX and Volume RAD exams without 0.2 mm Cu

<table>
<thead>
<tr>
<th></th>
<th>ESD [mGy]</th>
<th>E [mSv]</th>
<th>Monte Carlo</th>
<th>TLD</th>
<th>Literature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consolle</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ionization chamber</td>
<td>0.130 0.004</td>
<td>0.193 0.018</td>
<td>0.012 0.005</td>
<td>0.011 0.001</td>
<td>0.014-0.017</td>
</tr>
<tr>
<td>TLD</td>
<td>0.193</td>
<td>0.018</td>
<td>0.012 0.005</td>
<td>0.011 0.001</td>
<td>0.014-0.017</td>
</tr>
<tr>
<td>X-rays</td>
<td>0.181</td>
<td>0.113</td>
<td>0.193 0.018</td>
<td>0.012 0.005</td>
<td>0.011 0.001</td>
</tr>
<tr>
<td>DTS</td>
<td>1.723</td>
<td>1.233</td>
<td>1.630 0.163</td>
<td>0.140 0.056</td>
<td>0.135 0.014</td>
</tr>
<tr>
<td>CT</td>
<td>CTDlv = 7.2 mGy, DLP=319 mGy</td>
<td>4.9</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Different system gives comparable results
Cu filtration reduces dose
Dose comparison in SOS trial

<table>
<thead>
<tr>
<th>Mean effective dose (mSv)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Tomosynthesis</td>
<td>0.09</td>
</tr>
<tr>
<td>CT scan</td>
<td>4.9</td>
</tr>
</tbody>
</table>

Tomosynthesis delivers a dose 50 times lower

1) How does this affect accuracy?
2) How does this affect overall survival?
Dose comparison in screening programs

<table>
<thead>
<tr>
<th>Mean effective dose (mSv)</th>
<th>Tomosynthesis</th>
<th>Low dose CT screening scan</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.12</td>
<td>1.5; 3.8; 1.6-2.4; 1.5</td>
</tr>
</tbody>
</table>

Tomosynthesis deliver a dose <10 times lower but we could not compare accuracy and overall survival

1 Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening. The New England Journal of Medicine, June 29, 2011.
3 Estimated Radiation Dose Associated With Low-Dose Chest CT of Average-Size Participants in the National Lung Screening Trial. AJR Am J Roentgenol. 2011 Nov;197(5):1165-9
• Principle of digital tomosynthesis (DTS)
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Rationale

Lung cancer is the leading cause of cancer-related death around the world and the 12.7% of all new cancer diagnoses.

Clinical stage at diagnosis is a major determinant of survival after therapy. pathological stage 1 non-small cell lung cancer have a 5-years overall survival (58-73%) that is much larger than for all-comers (15%)

NLST open the way to CT screening for lung cancer (guidelines JTO) but must be weighed against the harms from positive screening results and overdiagnosis, as well as the costs

Hypothesis: DTS could be a an alternative to CT screening
SOS Study

Inclusion criteria:

Patients between 45 and 75 years old
Smokers or former smokers (pack*day*year
Former smokers should have stopped
  smoking no more than 10 years ago
No tumoral past pathology
No thoracic CT or PET in the last 2 years.
SOS protocol

- **No nodule or nodule < 5mm**
  - FU 1 year: DTS

- **Nodule > 5mm**
  - CT
    - Indeterminate
      - Not solid
        - FU 3 months: CT
      - Solid
        - PET-CT
    - Malign
      - Biopsy
Studies review

DTS images were blinded analysed by one chest radiologist (>20 years experience) and two residents radiologists.

Dishomogeneities in the review and positive studies were analysed on consensus session composed involving the 3 radiologists and 2 thoracic surgeons.

CT was considered as Gold Standard for defining positive nodules
Study demographics

1351 subjects

Dec 2010 – Dec 2011
70% smokers
27.9±21.1 cigarettes/day,
median 20
range 7-80

57.2±7.5 years,
median age 57 years
range of 45-75 years
35.5% were women
Study results: negative subjects

1351 subjects

1252 (92.7%) negative

979 no nodules

217 nodules smaller than 5 mm

56 with nodules calcified larger than 5mm

1year f-up DTS
Study results: positive subjects

1351 subjects

99 (7.3%) Positive
defined as nodules non calcified larger than 5mm

CT 25.2% CECT

90 (91%) TP

Work-up

10 lung cancer
56 negative, 21 not lung cancer, 10 in F-UP

9 (9%) FP
5 extra-thoracic
4 negative
## Lung cancer

8 resectable  
(60% stage I)  
2 not resectable  

<table>
<thead>
<tr>
<th>NEOPLASIA</th>
<th>stage</th>
<th>Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ca. sarcomatoide</td>
<td>I A</td>
<td>Lobectomy</td>
</tr>
<tr>
<td>Carcinoide</td>
<td>I A</td>
<td>Lobectomy</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>I A</td>
<td>Segmentectomy</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>I A</td>
<td>Lobectomy</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>I B</td>
<td>Lobectomy</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>I B</td>
<td>Lobectomy</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>III A</td>
<td>Segmentectomy</td>
</tr>
<tr>
<td>Maltoma</td>
<td>-</td>
<td>Atypical Resection</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>III B</td>
<td>NO</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>IV</td>
<td>NO</td>
</tr>
</tbody>
</table>
1 carcinoid

1 maltoma

1 ca. sarcomatoide

7 adenocarcinomas
Nodules analysis

221 nodules were detected by CT in the 99 subjects identified by DTS

<table>
<thead>
<tr>
<th>Nodule diameter</th>
<th>%</th>
<th>n.</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 3 mm - ≤ 5 mm</td>
<td>42</td>
<td>93</td>
</tr>
<tr>
<td>&gt; 5 mm - ≤ 8 mm</td>
<td>28</td>
<td>62</td>
</tr>
<tr>
<td>&gt; 8 mm - ≤ 10 mm</td>
<td>15</td>
<td>33</td>
</tr>
<tr>
<td>&gt;10 mm</td>
<td>15</td>
<td>33</td>
</tr>
<tr>
<td>&gt; 3 mm</td>
<td>100</td>
<td>221</td>
</tr>
</tbody>
</table>

PERCENTUALE DEI NODULI VISUALIZZATI IN TC IN BASE AL DIAMETRO

42%
28%
15%
15%
0%
5%
10%
15%
20%
25%
30%
35%
40%
45%

≥ 3 - ≤ 5 mm
>5 - ≤ 8 mm
>8 - ≤ 10 mm
>10 mm

> 3 mm
Detection rate of DTS is comparable to CT, particularly for nodules larger than 5 mm.
### DTS vs X-rays

<table>
<thead>
<tr>
<th></th>
<th>3-5 mm</th>
<th>5-8 mm</th>
<th>8-10 mm</th>
<th>&gt;10 mm</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>X-rays</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TP</td>
<td>10 11%</td>
<td>11 18%</td>
<td>11 33%</td>
<td>17 51%</td>
<td>49 22%</td>
</tr>
<tr>
<td>FP</td>
<td>9</td>
<td>8</td>
<td>9</td>
<td>16</td>
<td>42</td>
</tr>
<tr>
<td>DTS</td>
<td>37 40%</td>
<td>60 97%</td>
<td>33 100%</td>
<td>33 100%</td>
<td>163 74%</td>
</tr>
<tr>
<td>TP</td>
<td>37</td>
<td>60</td>
<td>33</td>
<td>33</td>
<td>163</td>
</tr>
<tr>
<td>FP</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>CT</td>
<td>93</td>
<td>62</td>
<td>33</td>
<td>33</td>
<td>221</td>
</tr>
</tbody>
</table>

TP rate is much higher in DTS respect to X-rays

FP rate is much lower in DTS respect to X-rays

Detection rate is comparable to CT, particularly for nodules larger than 5 mm
Nodules dimensions in CT and DTS were not significantly different ($p<0.01$)

$0.085 \pm 1.82$ mm
Conclusions

Preliminary results:

• The sensitivity for nodules detection is significantly higher in DTS respect to X-rays

• Detectability of DTS is almost comparable to that of CT for nodules larger than 5 mm

• Radiation exposure is at least 10 times lower than Low Dose CT
Thanks for the attention

This study has been supported by:

For inquiries e-mail to: chauvie.s@ospedale.cuneo.it
Case 1

Male
59 years old
Former smoker

DTS detected multiple nodules
Case 1

CT confirmed DTS findings
Case 1

PET-CT:
No captation
Follow-up CT at 3 months:
All nodules almost disappeared