Breast and Cervix Cancer: What are some ideas for providing the best care in 2019

David P. D’Souza
Associate Professor & Radiation Oncologist
• No conflicts of interest to declare
Breast Radiation and the Heart

Breast radiotherapy (RT) is a standard treatment option following breast conserving surgery.

- 1.7 fold increase in cardiac death with radiation compared to surgery alone.
- Increase in cardiac mortality in left-sided vs. right-sided treatment.
- Risk of ischemic heart disease increased proportionally to the mean heart dose.
Proportion of breast cancer patients with clinically significant heart disease 15 years post radiation

Clinically significant heart disease
- 59%

No clinically significant findings
- 41%

Clinically significant heart disease
- 8%

No clinically significant findings
- 92%

Standard fast helical CT (FH-CT)
of a left sided breast cancer patient

Left Ventricle (LV)
Left Anterior Descending (LAD)
Heart + Pericardium

Radiation Dose

- 50.0 Gy
- 45.0 Gy
- 40.0 Gy
- 32.5 Gy
- 25.0 Gy
- 10.0 Gy
Radiation Induced Ischemic Heart Disease

Macrovascular injury
acceleration of atherosclerosis

Ischemia

Microvascular injury
reduction in capillary density

2168 women between years of 1958 - 2001
Relative risk of ischemic heart disease of 1.33
No apparent dose threshold below which there is no risk.
Respiratory Induced Cardiac Motion via 4D-CT
Assessment of Intrafraction Breathing Motion on Left Anterior Descending Artery Dose During Left-Sided Breast Radiation Therapy

Omar El-Sherif, MSc, MD, Edward Yu, MD, Ilma Xhaferllari, BSc, DPhil, and Stewart Gaede, PhD

*Department of Medical Biophysics, University of Western Ontario; and Departments of Physics and Radiation Oncology, London Regional Cancer Program, London, Ontario, Canada

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Summary
Using 4-dimensional computed tomography (4D-CT) and deformable dose accumulation, we assessed the variation caused by breathing motion in the estimated dose to the left ventricle, left anterior descending artery, and left anterior descending artery (LAD) of left-sided breast cancer patients. The LAD showed substantial variation (±8.7 Gy) in dose due to breathing. In light of this, we suggest the use of 4D-CT and dose accumulation for future clinical studies looking at the relationship between LAD dose and cardiac outcome.

Purpose: To use 4-dimensional computed tomography (4D-CT) imaging to predict the level of uncertainty in cardiac dose estimates of the left anterior descending artery dose to the heart due to breathing motion during radiation therapy for left-sided breast cancer.

Methods and Materials: The fast helical CT (FH-CT) and 4D-CT of 30 left-sided breast cancer patients were retrospectively analyzed. Treatment plans were created on the FH-CT. The original treatment plan was then superimposed onto all 10 phases of the 4D-CT to quantify the dosimetric impact of respiratory motion through 4D dose accumulation (4D-dose). Dose-volume histograms for the heart, left ventricle (LV), and left anterior descending artery (LAD) were obtained from the FH-CT and compared with those obtained from the 4D-dose.

Results: The 95% confidence interval of 4D-dose and FH-CT differences in mean dose estimates for the heart, LV, and LAD were 6.0 Gy, 1.0 Gy, and 1.0 Gy, respectively.

Conclusion: Fast helical CT is a good approximation for doses to the heart and LV; however, dose estimates for the LAD are susceptible to uncertainties that arise due to intrafraction breathing motion that cannot be accounted for without the additional information obtained from 4D-CT and dose accumulation. For future clinical studies, we suggest the use of 4D-CT-derived dose-volume histograms for estimating the dose to the LAD. © 2016 Elsevier Inc. All rights reserved.
Results: Dose volume histogram for the left anterior descending artery (LAD)
Risk of Heart Toxicity

↑ Risk of RT induced heart disease:
• Total Dose (>30-35Gy)
• Fraction size (≥2Gy/day)
• Radiation source
• Volume of heart exposed
• Young age at treatment
• Increased time since treatment
• Co-existing coronary disease/risk
• Systemic treatment
Treatment Planning

Whole breast treatment field borders:
- Medial (mid-sternum)
- Lateral (mid-axillary)
- Superior (base of clavicular heads)
- Inferior (2cm below inframammary fold)
Treatment Planning

Breast planning considerations:

• Whole breast as target
• Normal organs to avoid: heart, lung, contralateral breast, liver
Breast planning considerations:

• Whole breast as target
• Normal organs to avoid: heart, lung, contralateral breast, liver
Not so good!
Treatment Planning
Breathing Control

• Voluntary or machine-regulated breath holds
• Causes a cession of breathing during the duration that the beam is on
• Commonly used when treating breast, lung, and esophageal cancer
• Techniques:
  – Deep-inspiration breath-holds (DIBH)
  – Active breathing control (ABC)
Deep-inspiration breath-holds (DIBH)

- Breathing instructions given
  - “Take a deep breath in, and hold it.”
- Beam is turned on during breath hold
- Patient instructed to breath when beam is turned off

- **Advantages:**
  - No additional equipment
  - Cost effective
  - Reduces tumor motion
  - Decrease in cardiac treated volumes ($V_{20}$ from 26.5 to 22.8 percent) and esophageal treated volumes ($V_{50}$ from 25.5 to 22.6 percent).\(^9\)
  - Increased doses and smaller tumor margins are possible

- **Disadvantages:**
  - Difficult to determine the breath hold reproducibility
  - Unrealistic for many elderly or frail patients, or those with pulmonary disease
Active Breathing Control (ABC)

- Mouthpiece placed in the patient’s mouth
  - Hooked up the ABC.
- Continuously monitors lung volume
- When the lung volume is at the ideal level, usually 70 to 80 percent of maximum inspiration, the valve on the mouthpiece is closed off
  - Prevents the patient from inhaling or exhaling.
  - Ensures breath hold reproducibility.
- The radiation beam is turned on, and once the radiation is finished being delivered, the valve is reopened, allowing the patient to resume breathing.

• **Advantages:**
  - Guarantees reproducible breath holds
  - Reduces tumor motion and cardiac and esophageal treated volumes
• **Disadvantages:**
  - More invasive
  - Patient needs to hold their breath for a minimum of 15 seconds\(^6,8\)
  - May require verbal training by the therapist
Real-Time Tracking

• Real time tumor localizations
  – Techniques to track tumor position:
    • External respiratory surrogates
    • Implanted radio-opaque fiducial markers
    • Surface imaging

• Once the tumor is accurately located, the radiation beam will turn on and begin treating

• Examples:
  – Real-time Position Management (RPM) System, AlignRT
Real-Time Position Management System

- Utilizes an **external respiratory surrogate**
  - A plastic box with infrared reflective markers
  - Placed on top of the patient’s abdominal surface
- Infrared cameras detect the reflective markers
- During treatment, the tumor is tracked
  - When the respiratory location matches the location predetermined, the beam will turn on.
  - When out of the assigned location, the beam turns off
AlignRT

- **Surface imaging**
  - Uses two infrared cameras to triangulate the location of the patient and derive depth information
  - In order to precisely locate the patient position, an optical pattern is projected onto the patient to identify the corresponding points
  - An algorithm uses the points to create a surface image of the patient.
  - From the surface image, the therapists can then make shifts to align the image to the original planning image.
  - Throughout the entire treatment, AlignRT tracts the motion, and only allows the continuation of treatment when the tumor location is within the assigned tolerance location.
Real-Time Tracking

• **Advantages:**
  – Accurate tracking of the tumor.
  – Intrafractional movement regulation.
  – Non-invasive and excludes rigid frames.
  – Eliminates patient discomfort
  – Requires no active patient participation.
  – Patient receives no additional radiation dose.
    • Infrared laser use

• **Disadvantages**
  – Significantly increased treatment times
  – Tumor motion must be assumed to match the surface motion, unless the system uses internal markers.
Conclusions

• Respiratory motion management in combination with breathing control is beneficial in the reduction of *intra*fractional motion
• Allows for a decrease in treatment volumes, resulting in a reduction of normal tissue toxicities while giving higher doses to the lesion
• Still recommended to use *inter*fractional imaging
Active breathing control (ABC)

- ABC device uses a spirometry system
- Patients breathe through mouth piece
- Spirometry valve stops airflow after reaching the predetermined inspiration threshold

Slides courtesy of Grace Lee from Princess Margaret Cancer Centre, Toronto
Active breathing control to achieve cardiac dose reduction

(Wang et al. IJROBP 2012)
Active breathing control to achieve cardiac dose reduction

Breath-hold
Active breathing control to achieve cardiac dose reduction

(Wang et al. IJROBP 2012)
Dose Volume Histogram

(Wang et al., IJROBP 2012)
## Cardiac dose reduction

<table>
<thead>
<tr>
<th></th>
<th>Free Breathing</th>
<th>ABC Breath-hold</th>
<th>Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Volume in radiation field</td>
<td>29.9cc</td>
<td>3.7cc</td>
<td>88%</td>
</tr>
<tr>
<td>Mean Dose</td>
<td>317cGy</td>
<td>132cGy</td>
<td>59%</td>
</tr>
<tr>
<td>Left Anterior Descending</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max Dose</td>
<td>4155cGy</td>
<td>1507cGy</td>
<td>64%</td>
</tr>
<tr>
<td>Mean Dose</td>
<td>2047cGy</td>
<td>594cGy</td>
<td>71%</td>
</tr>
</tbody>
</table>
Breathing Adapted RT

• The heart is a radiosensitive organ
• Use of a breath hold system in left-sided breast RT significantly reduces dose to the heart and LAD
• Approximately 30% of all left-sided breast RT patients will benefit from this technique
• ABC technique is well accepted by patients and staff, results in only moderate increase in workload and additional resources
• ABC is now standard practice at the PMH
What did we do?

• Breast radiation treatments comprise a significant proportion of treatment time on the radiation machines

• Inertia
  – Things work well scheduling patients on treatment units
  – Staff are comfortable and well trained to deliver treatments as is
  – What happens to wait times, the cost etc?
Supine, Gated, Deep Inspiration Breath-Hold

Same patient, free breathing versus Gated, Deep Inspiration Breath-Hold
We have the capabilities of Gated, Deep Inspiration breath-Hold on the Four TrueBeam Units
Prone, Free Breathing Technique

Same patient, Prone versus Supine
Four new Aktina Prone Breast Boards are being shipped today!
We have good experience treating Signal Breasts Prone with great accuracy.
## Comparing Two Techniques: Advantages of Prone Technique over Supine, Gated, Deep Inspiration Breath-Hold

<table>
<thead>
<tr>
<th>PRONE, FREE BREATHING</th>
<th>SUPINE, GATED, DEEP INSPIRATION BREATH-HOLD</th>
</tr>
</thead>
<tbody>
<tr>
<td>• No Gating required, all units capable</td>
<td>• Requires Gating on TrueBeam</td>
</tr>
<tr>
<td>• No special patient education or coaching required</td>
<td>• Requires patient education, coaching and compliance</td>
</tr>
<tr>
<td>• No beam interruption during treatment</td>
<td>• Beam on during inspiration only</td>
</tr>
<tr>
<td>• Minimal staff training required</td>
<td>• Considerable staff training needed</td>
</tr>
<tr>
<td>• Ability to hold breath not necessary</td>
<td>• Subset of patients unable to perform inspiration breath hold</td>
</tr>
</tbody>
</table>
### Comparing Two Techniques: Advantages of Prone Technique over Supine, Gated, Deep Inspiration Breath-Hold

<table>
<thead>
<tr>
<th>SUPINE, GATED DEEP INSPIRATION BREATH-HOLD</th>
<th>PRONE, FREE BREATHING</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Most patient are comfortable and stable lying supine</td>
<td>• Many patients have difficulty lying prone and are less stable (tend to roll)</td>
</tr>
<tr>
<td>• Treatment fields visible on skin</td>
<td>• For larger patients it is difficult to displace upper abdominal fatty tissue away from the inferior mammary fold.</td>
</tr>
<tr>
<td>• Staff familiar with supine technique.</td>
<td>• Difficult to visualize treatment fields on skin.</td>
</tr>
<tr>
<td></td>
<td>• Staff are less familiar with prone breast than supine treatment.</td>
</tr>
<tr>
<td></td>
<td>• Supraclav. difficult to match when treating prone</td>
</tr>
</tbody>
</table>
Considerations in Developing and Implementing Gated Breath Hold Technique:

1. What is the patient population? Initial population versus ideal population?

2. How deep and for how long should patients be coached to hold their breath?

3. How useful would a visualization device be, for patients to self-monitor their breathing during treatment?

4. What education should be given to Therapists to best coach patients for breath hold. Should we have a site visit?

5. How should the patients best be educated for voluntary breath-hold. Do we need an additional appointment prior to CT?
6. How large should the gated window be?

7. What QA is required during treatment delivery? Should we take images for verification during treatment?

8. What is the IGRT protocol?

9. Is a mock setup required on day one?

10. Will we treat tangents only? Are there any issues with matching the supraclavicular fossa with deep inspiration breath-hold?
Clinical Implementation of 4D-CT for Left-Sided Breast Cancer

• All patients receive a fast-helical CT used for radiation dose calculation
• Followed by a 4D-CT
• Therapists determine the end inhale and end exhale phases of the respiratory cycle
• Transfer all 3 CT datasets to Pinnacle

Courtesy of Stew Gaede
Other Methods to Account for respiratory motion

4D-CT

Respiratory Gating At End Inhalation

Deep Inspiration Breath Hold

- Add margins
- Perform 4D-CT dose calculation
# Volumetric Modulated Arc Therapy (VMAT)

<table>
<thead>
<tr>
<th>Type of Radiation Delivery</th>
<th>Mean Dose to Heart (cGy)</th>
<th>V40 (%)</th>
<th>V5 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forward IMRT</td>
<td>1891.2</td>
<td>29.83</td>
<td>50.78</td>
</tr>
<tr>
<td>VMAT</td>
<td>819.2</td>
<td>3.34</td>
<td>42.92</td>
</tr>
</tbody>
</table>

VMAT (Volumetric Modulated Arc Therapy) Standard Technique
Respiratory Motion and VMAT for treating Breast Cancer

Figure 1. Mean Heart Dose for VMAT Plans

- DIBH vs. FH – p<0.05
- FH vs. 0% - p<0.05
- DIBH vs. 0% - p<0.05

Figure 2. V₃₀ of the Heart for VMAT Plans

- DIBH vs. FH – p<0.05
- FH vs. 0% - p>0.05
- DIBH vs. 0% - p<0.05

In-house study
• Higher V5 values for VMAT plans

DIBH vs. FH – p<0.05
FH vs. 0% - p>0.05
DIBH vs. 0% - p<0.05
Clinical Implementation of DIBH for Left–Sided Breast Cancer

- All patients receive:
  - Fast-helical CT with DIBH
  - 4D–CT
    - Full length (not just heart)

- Quick assessment of heart involvement with 4D–CT

- If significant, then plan with DIBH

- If not significant, then use 4D–CT (free–breathing)
  - Fuse 0% and 50% (or 60%) to untagged average

- VMAT can be used for either scenario (ie IMC involvement, bi–lateral, etc)
Clinical Implementation of DIBH for Left-Sided Breast Cancer

- Truebeam allows for DIBH CBCT
  - Apples to apples comparison with planning CT

- EPID in cine mode
  - During treatment verification ensures heart is out of field
QuickStart Radiotherapy: A Multidisciplinary Approach to Same-Day Radiotherapy Treatment

Courtesy of Grace Lee, Princess Margaret Cancer Centre
Rationale

• Catchment area for referrals is as much as 4 hours’ drive
• While we are increasing the number of telemedicine (videoconferencing) consults, there is no way to perform radiation planning remotely
• Improve radiation utilization (and breast conservation therapy) rates
Multi-disciplinary Team

Radiation Oncologist
- Patient selection
- Target delineation + Plan review and approval

Clinical specialist radiation therapist
- Patient triage
- Cavity target delineation (RO review/approval)
- Patient education and support

Physicist
- Development/integration of automated planning software

Dosimetrist/Planner
- Utilization of automated planning software

Treatment Therapist
- QA and Treatment
QuickStart Process

1-3 days

Radiation Oncology Consultation (Decision to Treat) → CT Simulation

Target Delineation ← Image Import

1-3 days

Planning/Publishing → Plan Approval: Physics/RO

2-10 days

Plan Approval: Physics/RO ← QA

2-10 days

Treatment ← Planning/Publishing
QuickStart Process

Radiation Oncology Consultation (Decision to Treat)

CT Simulation Image assessed by CSRT

1-3 days

CSRT Target Delineation + RO approval

Image Import

Automated planning/Publishing

Plan Approval: Physics/RO

Treatment

QA
<table>
<thead>
<tr>
<th>QuickStart Radiation Treatment Procedure</th>
<th>Wait Time [hour:min]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n = 73</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Target Delineation</strong></td>
<td>Median (range)</td>
</tr>
<tr>
<td></td>
<td><strong>0:23 (0:05-1:02)</strong></td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
</tr>
<tr>
<td></td>
<td><strong>0:25 (0:12)</strong></td>
</tr>
<tr>
<td><strong>Plan Completion by Planner</strong></td>
<td>Median (range)</td>
</tr>
<tr>
<td></td>
<td><strong>0:56 (0:21-2:56)</strong></td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
</tr>
<tr>
<td></td>
<td><strong>1:02 (0:29)</strong></td>
</tr>
<tr>
<td><strong>Physics + Radiation Oncology Approvals</strong></td>
<td>Median (range)</td>
</tr>
<tr>
<td></td>
<td><strong>0:23 (0:03-1:21)</strong></td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
</tr>
<tr>
<td></td>
<td><strong>0:28 (0:16)</strong></td>
</tr>
<tr>
<td><strong>Radiation Therapy Quality Checks</strong></td>
<td>Median (range)</td>
</tr>
<tr>
<td></td>
<td><strong>0:33 (0:09-1:54)</strong></td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
</tr>
<tr>
<td></td>
<td><strong>0:34 (0:19)</strong></td>
</tr>
<tr>
<td><strong>CT simulation to RT treatment</strong></td>
<td>Median (range)</td>
</tr>
<tr>
<td></td>
<td><strong>2:45 (1:32-4:04)</strong></td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
</tr>
</tbody>
</table>
|                                                                           | **2:42 (0:30)**
<table>
<thead>
<tr>
<th>Wait Times Prior to Breast Radiotherapy Treatment [days]</th>
<th>QuickStart n = 25</th>
<th>Conventional n = 25</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Last Surgery/Chemotherapy to RO Consult</td>
<td>Median (range)</td>
<td>35 (7-77)</td>
<td>35 (11-81)</td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>32 (15)</td>
<td>39 (19)</td>
</tr>
<tr>
<td>Last Surgery/Chemotherapy to RT Treatment</td>
<td>Median (range)</td>
<td>38 (20-79)</td>
<td>60 (31-104)</td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>43 (17)</td>
<td>61 (21)</td>
</tr>
<tr>
<td>RO consultation to RT Treatment</td>
<td>Median (range)</td>
<td>7 (0-35)</td>
<td>20 (7-46)</td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>10 (11)</td>
<td>21 (10)</td>
</tr>
<tr>
<td>Consent to RT Treatment</td>
<td>Median (range)</td>
<td>2 (0-11)</td>
<td>16 (7-46)</td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>2 (3)</td>
<td>19 (11)</td>
</tr>
</tbody>
</table>
QuickStart

- All same day QuickStart patient were treated in advance of the 14-day Ontario wait-time guideline
- No clinical deficiencies identified any of the QuickStart plans (QA Rounds)
- No error incidences reported for any patients treated through the QuickStart process
Benefits of QuickStart

Institution
- Expedited simulation and treatment process
  - Average wait-time of 2 hours 50 mins
  - Patient waits by 11 days
  - Recover time lost to previous delays in patient’s cancer journey

Patients
- Back to their work and family life sooner
- Less of a financial burden on patients
CERVIX CANCER
Epidemiology

• Cervix cancer is the 4th most common cancer in females worldwide
• Estimated in 2018 - 570,000 new cases
• In contrast 1550 cases and 400 deaths projected for 2018 by CCS
Screening

• Canadian Task Force on Preventative Health Care Screening Guidelines of 2013
  • For women aged 30 to 69 we recommend routine screening for cervical cancer every 3 years
  • (Strong recommendation; high quality evidence)
Minimally invasive surgery

• Several advantages often cited:
  – Small incisions
  – Less pain
  – Low risk of infection
  – Short hospital stay
  – Quick recovery time
  – Less scarring
  – Reduced blood loss
Minimally Invasive versus Abdominal Radical Hysterectomy for Cervical Cancer
• METHODS

• In this trial involving patients with stage IA1 (lymphovascular invasion), IA2, or IB1 cervical cancer

• squamous-cell carcinoma, adenocarcinoma, or adenosquamous carcinoma

• randomly assigned patients to undergo minimally invasive surgery or open surgery
• **METHODS**

• The primary outcome was the rate of disease-free survival at 4.5 years

• Non-inferiority claimed if the lower boundary of the two-sided 95% confidence interval of the between-group difference (minimally invasive surgery minus open surgery) was greater than −7.2 percentage points (i.e., closer to zero).
• 319 patients were assigned to minimally invasive surgery and 312 to open surgery.
• MIS: 84.4% underwent laparoscopy and 15.6% robot-assisted surgery
• Overall, the mean age of the patients was 46.0 years. Most patients (91.9%) had stage IB1 disease.
• Groups were similar with respect to histologic subtypes, the rate of lymphovascular invasion, rates of parametrial and lymph-node involvement, tumor size, tumor grade, and the rate of use of adjuvant therapy.
• DFS at 4.5 years was 86.0% with MIS and 96.5% with open surgery, a difference of −10.6 percentage points (95% confidence interval [CI], −16.4 to −4.7).

<table>
<thead>
<tr>
<th>Population</th>
<th>Disease-free Survival Rate at 4.5 Yr (95% CI)</th>
<th>Difference (95% CI)</th>
<th>P Value for Noninferiority</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Minimally Invasive Surgery</td>
<td>Open Surgery</td>
<td></td>
</tr>
<tr>
<td>Intention-to-treat population</td>
<td>86.0 (79.7–90.4)</td>
<td>96.5 (92.7–98.4)</td>
<td>0.87</td>
</tr>
<tr>
<td>Per-protocol population</td>
<td>87.1 (81.0–91.3)</td>
<td>97.6 (94.1–99.0)</td>
<td>0.88</td>
</tr>
</tbody>
</table>

A

B

Hazard ratio for disease recurrence or death from cervical cancer, 3.74 (95% CI, 1.63–8.58)
P = 0.002
MIS was associated with a lower rate of disease-free survival than open surgery (3-year rate, 91.2% vs. 97.1%; hazard ratio for disease recurrence or death from cervical cancer, 3.74; 95% CI, 1.63 to 8.58), a difference that remained after adjustment for age, body-mass index, stage of disease, lymphovascular invasion, and lymph-node involvement; minimally invasive surgery
• MIS also associated with a lower rate of overall survival (3-year rate, 93.8% vs. 99.0%; hazard ratio for death from any cause, 6.00; 95% CI, 1.77 to 20.30).
Locoregional recurrence

Hazard ratio for locoregional recurrence, 4.26 (95% CI, 1.44–12.60)

Cumulative Incidence of Locoregional Recurrence (%)

No. at Risk
- Open surgery: 312, 280, 236, 187, 163, 144, 134, 123, 104, 90, 7
- Minimally invasive surgery: 319, 292, 244, 192, 167, 155, 142, 121, 102, 80, 5

Years since Randomization

Years: 0, 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0, 4.5, 5.0

Graph showing cumulative incidence of locoregional recurrence with hazard ratio.
INCIDENCE OF ADVERSE EVENTS COMPARING ABDOMINAL VS. MINIMALLY INVASIVE RADICAL HYSTERECTOMY IN PATIENTS WITH EARLY-STAGE CERVICAL CANCER: LACC TRIAL

A. Obermair, R. Asher, M. Frumovitz, R. Pareja, A. Lopez

IGCS 2018, Kyoto, Japan
Methods:

• For this analysis, compared the incidence of AEs between TARH and MIRH up to 6 weeks post-op

• AEs were graded according to Common Toxicity Criteria (Ver 3). Major AEs were CTC grade 3+ or Serious AEs.

• Also defined presurgical characteristics associated with the risk of an AE.
Results:

A total of 573 patients underwent surgery of which 571 had a minimum of 6-weeks follow-up (274 TARH vs. 297 MIRH) and were included in this analysis.

Patient characteristics were similar between the two arms.

The proportion of intraoperative, postoperative and major AEs between treatment arms was similar.

No difference in the rate of GI, GU or lymphocyst/lymphocele complications.

TARH was associated with greater intra-operative blood loss (p<0.001) and higher rate of blood transfusions (p=0.03).
<table>
<thead>
<tr>
<th></th>
<th>TARH</th>
<th>MIRH</th>
<th>p-value**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraoperative AEs</td>
<td>28 (10%)</td>
<td>34 (11%)</td>
<td>0.63</td>
</tr>
<tr>
<td>Postoperative AEs* (CTC grade 2+)</td>
<td>104 (38%)</td>
<td>115 (39%)</td>
<td>0.82</td>
</tr>
<tr>
<td>Any GI</td>
<td>36 (13%)</td>
<td>37 (12%)</td>
<td>0.82</td>
</tr>
<tr>
<td>Any urinary</td>
<td>104 (38%)</td>
<td>114 (38%)</td>
<td>0.89</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>22 (8%)</td>
<td>11 (4%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Return to operating theatres</td>
<td>9 (3%)</td>
<td>15 (5%)</td>
<td>0.30</td>
</tr>
<tr>
<td>Operative time (minutes)</td>
<td>196.8 (60.6)</td>
<td>226.2 (69.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Blood loss (ml)</td>
<td>200 (0 - 2200)</td>
<td>100 (0 - 1500)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*up to six week post-operatively; **based on a Chi-squared test
QUALITY OF LIFE ASSESSMENT IN EARLY-STAGE CERVICAL CANCER PATIENTS IN UNDERGOING RADICAL HYSTERECTOMY VIA MINIMALLY INVASIVE SURGERY OR OPEN APPROACH: THE LACC TRIAL

M. Frumovitz, et al

IGCS 2018, Kyoto, Japan
• **Methods:**

• Patients participating in this phase III randomized, international study completed validated quality of life (QoL) and symptom assessments (SF-12, FACT-Cx, EQ-5D, and MDASI) before surgery, at 1 and 6 weeks, and at 3 and 6 months after surgery.

• Differences in QoL over time between treatment arms were assessed using generalized estimating equations.
Results:

- Similar numbers in each arm completed instruments
- SF-12 there was no significant difference between the two arms at any time point for the physical or mental components scores
- FACT-Cx total scores for physical, functional, social, or emotional well-being were similar between the 2 arms at all-time points
- EQ-5D a higher proportion of patients who underwent open surgery had mobility problems at 1 week post-surgery compared to patients who had MIS (p<0.001), however by 6 weeks there was no longer a significant difference
- No difference at any time point for any of the other 5 subscales of the EQ-5D (self-care, usual activities, pain/discomfort, and anxiety/depression)
- Acute symptoms as assessed by the MD Anderson Symptom Index (MDASI) were similar between the 2 arms at all-time points
• Appreciation that cervix cancer is not a “one size fits all” treatment with radiotherapy as has been traditionally considered
• 4 field box radiation
• Film based brachytherapy
4 field box radiation

Schematic diagram depicting nodal coverage with the 4-field box in the (A) AP-PA fields and (B) lateral fields.
Is planning of films or digital fluoroscopy good enough?
Going from 2D to 3D

• Be aware of dynamic nature of the body:
  • Organs at risk change (shape/filling, position)
• Tumour moves, regresses
Multi-centre prospective trial, STIC done in France showed @ 24 months, Grade 3/4 toxicity between 2D and 3D cervix brachytherapy to be 22.7% versus 2.6%

Charra-Brunaud C, Radiother Oncol 2012
Gyn GEC ESTRO Guidelines

- Concepts and terms in 3D image-based treatment planning
- Includes 3D volume parameters, aspects of 3D image-based anatomy, radiation physics and radiobiology
- Based on consensus workshops considering Point A and ICRU 38 nomenclature

Pötter et al Radiother Oncol 2005
MR guided cervix brachytherapy

• MR imaging, when performed with adequate imaging protocols, meets the demands for 3D image-based BT for cervical cancer.
• It provides essential information about tumour extent, topography and regression, as well as topography of patho-anatomical structures.
• ...provided information helpful to reduce uncertainties regarding the definition of GTV, CTVs and patho-anatomical structures.

Dimopoulos J et al Radiother Oncol 2012 (Gyn GEC-ESTRO WG)
• Use of MR guided cervix brachytherapy is fully endorsed by the “experts”
  – GEC-ESTRO
  – Canadian experts (Croke et al Pract Rad Oncol 2016)
  – Cancer Care Ontario Gyn RO Community of Practice
• Results of 731 patients from retroEMBRACE (12 institutions)
• 3/5 year LC 91%/89%
• Low serious morbidity

Sturdza A et al. Radiother Oncol 2016
Clinical Drawing

Patient:

At Diagnosis
At Brachytherapy
EBRT Gy

Infiltrative Exophytic

Cervix
Vagina
Parametria
Rectum or Bladder

w = __ cm
h = __ cm
t = __ cm
Vagina Involvement = __ cm

dd/mm/yy
“Hybrid” Interstitial

Week 1: Ovoids with Tandem

Week 2: Hybrid Interstitial
• One of the benefits of Pap testing is a significant reduction in death rates in developed countries like Canada
• Some areas have **HPV co-testing** (Ontario the patient pays for it still) that may better select women at higher risk
• **HPV vaccine**
While we have some work to do on convincing the anti-vaxxers, there overall is a greater sense that we’ve got things under control.
CERVICAL CANCER: STOP THE STIGMA

Let's Get Real... The Facts

90% of cervical cancers are associated with human papillomavirus (HPV), a sexually transmitted disease.

Women with more than one sexual partner are not the only ones susceptible to cervical cancer.

HPV is extremely prevalent. Most sexually active women and men will contract it at some point in their lives— even those who only have one sexual partner.

We must work together to stop the stigma.

Why?

We need to talk openly about this life-threatening disease to prevent it.

131.95 million women in the U.S. over the age of 15 are at risk of developing cervical cancer.

In 2016 about 12,990 new cases of invasive cervical cancer will be diagnosed and roughly 4,120 women will lose their lives to cervical cancer.

Hope for a Cure

There is hope for women battling cervical cancer and those that have yet to be diagnosed.

Practice Prevention

- Get a pap test regularly to catch cervical cancer early.
- Get screened for HPV.
- Get an HPV vaccine.
- Use protection if you're sexually active.
- Don't smoke.

Ladies — let's stop the stigma. Talk to a friend about prevention today!

Visit swhr.org
to learn more, seek support, and raise awareness for the brave women battling cervical cancer!
Or do we?

30 weeks, 3 days gestation
• Clinical experience suggests that there woman who present with locally advanced cervix cancer despite following recommended Pap smear screening

• Performed qualitative research to study patient’s symptoms prior to diagnosis, experience with the health care system etc.
• Looked at **women under 50** with locally advanced cervix cancer (LACC), Stages 1B1 to 4A undergoing curative chemoradiation
• Who had a Pap smear within the 2 years preceding diagnosis
• Invited to semi-structured, in-person interview with non-physician
• Data recorded, transcribed; thematic analysis performed
• Over 2 year period, 13/38 women had Pap screening done
• Ten consented to participate in an interview
• We identified 6 themes
• Belief that LACC does not occur in screening compliant patients
• Lack of understanding about the symptoms/diagnosis of cervix cancer
• Reluctance from health care providers to perform a detailed pelvic examination in the presence of symptoms
• Negative emotions including anger, shame, regret, and mistrust
• Changes in quality of life from treatment
• Advice to other women to advocate more strongly when something seems wrong
Summary

• Cardiac dose from left sided breast radiation is of clinical importance
• There is a rationale to reduce the cardiac dose by a number of methods
• Our success with implementation came after buy in from all stakeholders
• Some of the innovation in health care can come from people (using technology) to allow same day radiation start for breast cancer to improve access
• Newer technology is not always better; MIS for cervix cancer is actually worse despite the appeal of using a robot or laparoscope

• While there are advances expected with precision radiation (MR guided brachytherapy) and the HPV vaccine, there is a need to educate all about the signs and symptoms of cervix cancer