

XXIII CONGRESSO  
**AIRO2013**

Giardini Naxos - Taormina, 26 - 29 ottobre

## **Can FDG-PET Predict Clinical Response and DFS after radio-brachytherapy in Cervix Cancer ?**

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Acta Oncologica Symposium

**Biology-Guided Adaptive Radiotherapy**

Aarhus, Denmark - June 11-13, 2013

# Background:

## Metabolic Response on Posttherapy FDG-PET Predicts Patterns of Failure After Radiotherapy for Cervical Cancer

Julie K. Schwarz, M.D., Ph.D.,<sup>\*,†</sup> Barry A. Siegel, M.D.,<sup>\*,†</sup> Farrokh Dehdashti, M.D.,<sup>\*,†</sup> and Perry W. Grigsby, M.D., M.B.A.<sup>\*,†,‡,§</sup>

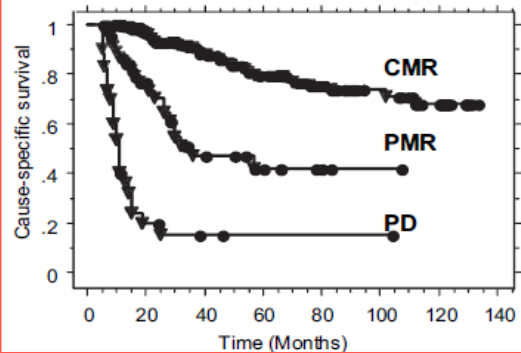


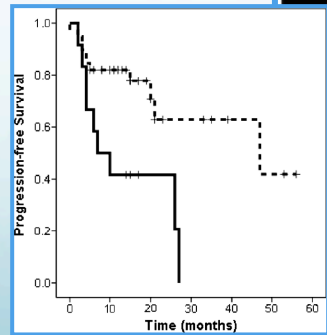
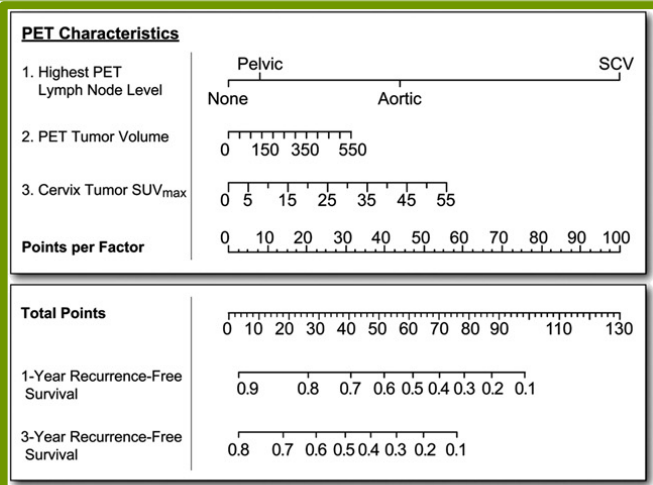
Table 3 Patterns of failure and metabolic response

|                         | Complete metabolic response (n = 173) | Partial metabolic response (n = 40) | Progressive disease (n = 25) | Total (n = 238) |
|-------------------------|---------------------------------------|-------------------------------------|------------------------------|-----------------|
| Pelvis                  | 6                                     | 15                                  | 1                            | 22              |
| Distant                 | 29                                    | 5                                   | 15                           | 49              |
| Both pelvis and distant | 5                                     | 6                                   | 9                            | 20              |
| <b>Total</b>            | <b>40 (23%)</b>                       | <b>26 (65%)</b>                     | <b>25 (100%)</b>             | <b>91 (38%)</b> |

**p < .0001**

Gynecologic Oncology  
journal homepage: [www.elsevier.com/locate/yygyno](http://www.elsevier.com/locate/yygyno)

FDG-PET-based prognostic nomograms for locally advanced cervical cancer  
Elizabeth A. Kidd<sup>a</sup>, Issam El Naqa<sup>b</sup>, Barry A. Siegel<sup>c,d</sup>, Farrokh Dehdashti<sup>c,d</sup>, Perry W. Grigsby<sup>c,d,e,f,\*</sup>



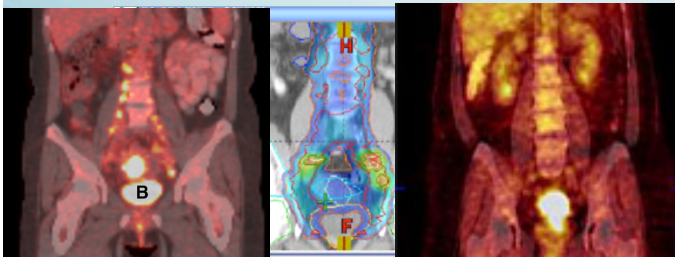
<sup>18</sup>F-Fluoro-2-Deoxy-D-Glucose Positron Emission Tomography Standard Uptake Value Ratio as an Indicator of Cervical Cancer Chemoradiation Therapeutic Response  
Charles Kinos, MD, PhD,<sup>\*</sup> Tomas Radivoyevitch, PhD,<sup>†</sup> Fadi W. Abdul-Karim, MD,<sup>‡</sup> and Peter Faulhaber, MD<sup>§</sup>

Post-PreRatio: 0.08

Post-PreRatio: 0.58

# Hypothesis:

1. *Pretreatment* Metabolic volume and SUVmax predict outcome (DFS) in cervix cancer
2. Clinical response 2-3 months after treatment is a early surrogate of Disease Free Survival and Overall survival
2. SUV ratio (pre/postt) and SUV posttreatment are better clinical response predictor then SUVmax pretreatment



# Material & Methods:

## *Patients characteristics*

- Pts evaluated:  
underwent PETCT  
(treated between 2006  
and 2012)
- 82 pts with baseline  
fdgPETCT
- 48 baseline and post  
treatment

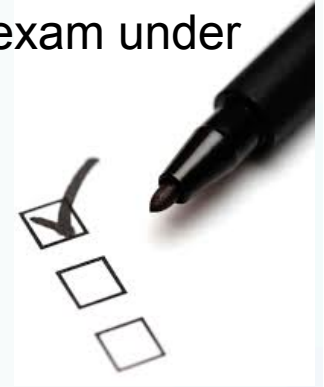
| Variable                  | Pre-RT Scan only<br>(N = 82) |        | Pre+ Post -RT Scan<br>(N = 48) |        |
|---------------------------|------------------------------|--------|--------------------------------|--------|
|                           | N                            | [%]    | N                              | [%]    |
| <b>FIGO status</b>        |                              |        |                                |        |
| IB                        | 10                           | [12.2] | 2                              | [4.2]  |
| IIA                       | 8                            | [9.8]  | 3                              | [6.3]  |
| IIB                       | 49                           | [59.8] | 33                             | [68.8] |
| IIIA                      | 1                            | [1.2]  | 1                              | [2.1]  |
| IIIB                      | 9                            | [11.0] | 7                              | [14.6] |
| IVA                       | 5                            | [6.1]  | 2                              | [4.2]  |
| <b>Bulky tumour</b>       |                              |        |                                |        |
| No                        | 22                           | [26.8] | 10                             | [20.8] |
| Yes                       | 60                           | [73.2] | 38                             | [79.2] |
| <b>Lymph Nodal Status</b> |                              |        |                                |        |
| Negative                  | 51                           | [62.2] | 27                             | [56.3] |
| Positive                  | 31                           | [37.8] | 21                             | [43.8] |
| <b>Hystology</b>          |                              |        |                                |        |
| Squamous Cell Carcinoma   | 68                           | [82.9] | 39                             | [81.3] |
| Adenocarcinoma            | 8                            | [9.7]  | 6                              | [12.5] |
| Adenosquamous Carcinoma   | 4                            | [4.9]  | 2                              | [4.1]  |
| Large Cell Carcinoma      | 2                            | [2.4]  | 1                              | [2.0]  |
| <b>Age [years]</b>        |                              |        |                                |        |
| Median                    | 55.9                         |        | 55.5                           |        |
| Range                     | 29.3 - 89.2                  |        | 29.3 - 88.3                    |        |



## Material & Methods: *Patients characteristics*

- **Baseline:** Pts underwent clinical evaluation, including a gynaecologic exam under anaesthesia, MR imaging, fdgPETCT

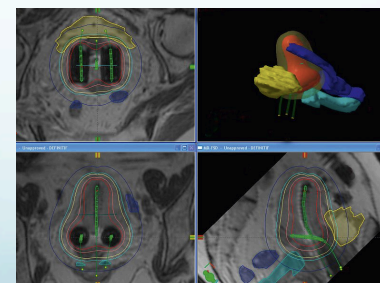
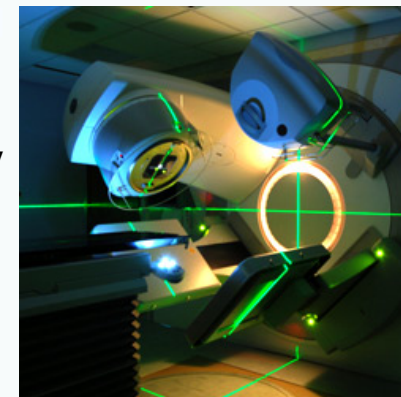
- **Treatment**



# Material & Methods:

## *Treatment Summary*

- External beam =
  - Pelvic radiotherapy (lower para-aortic LN irradiation for bulky tumours and/or N+) delivering 45-50.4 Gy with conventional fractionation.
  - N+ → additional boost of 16.2 Gy in 9 daily fractions.
- Pelvic radiotherapy was combined with either weekly cisplatin (40 mg/m<sup>2</sup>) or deep hyperthermia (except for non-bulky tumours FIGO stage ≤ IIA).
- Until 2009= HDR-brachytherapy with 3-4 fractions of 7 Gy to point A was applied.
- Since 2009= MR-image guided adaptive brachytherapy was applied (GEC-ESTRO guidelines → EQD2 dose of at least 85Gy to 90% of the high risk CTV)



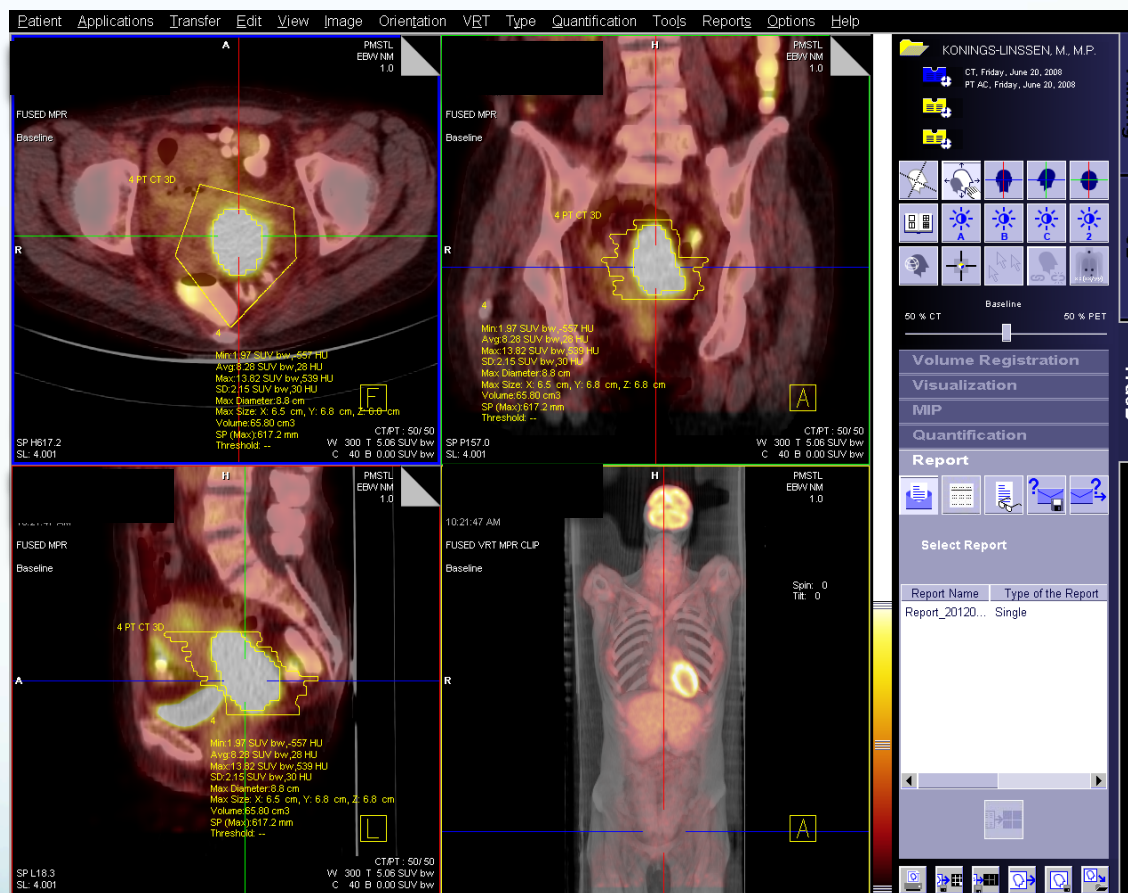
## Material & Methods: *Patients characteristics*

- **Baseline:** Pts underwent clinical evaluation, including a gynaecologic exam under anaesthesia, MR imaging, fdgPETCT
- **Treatment**
- **2-3 months** after treatment, pts underwent clinical re-evaluation, MR imaging, fdgPETCT (only in 48 pts)

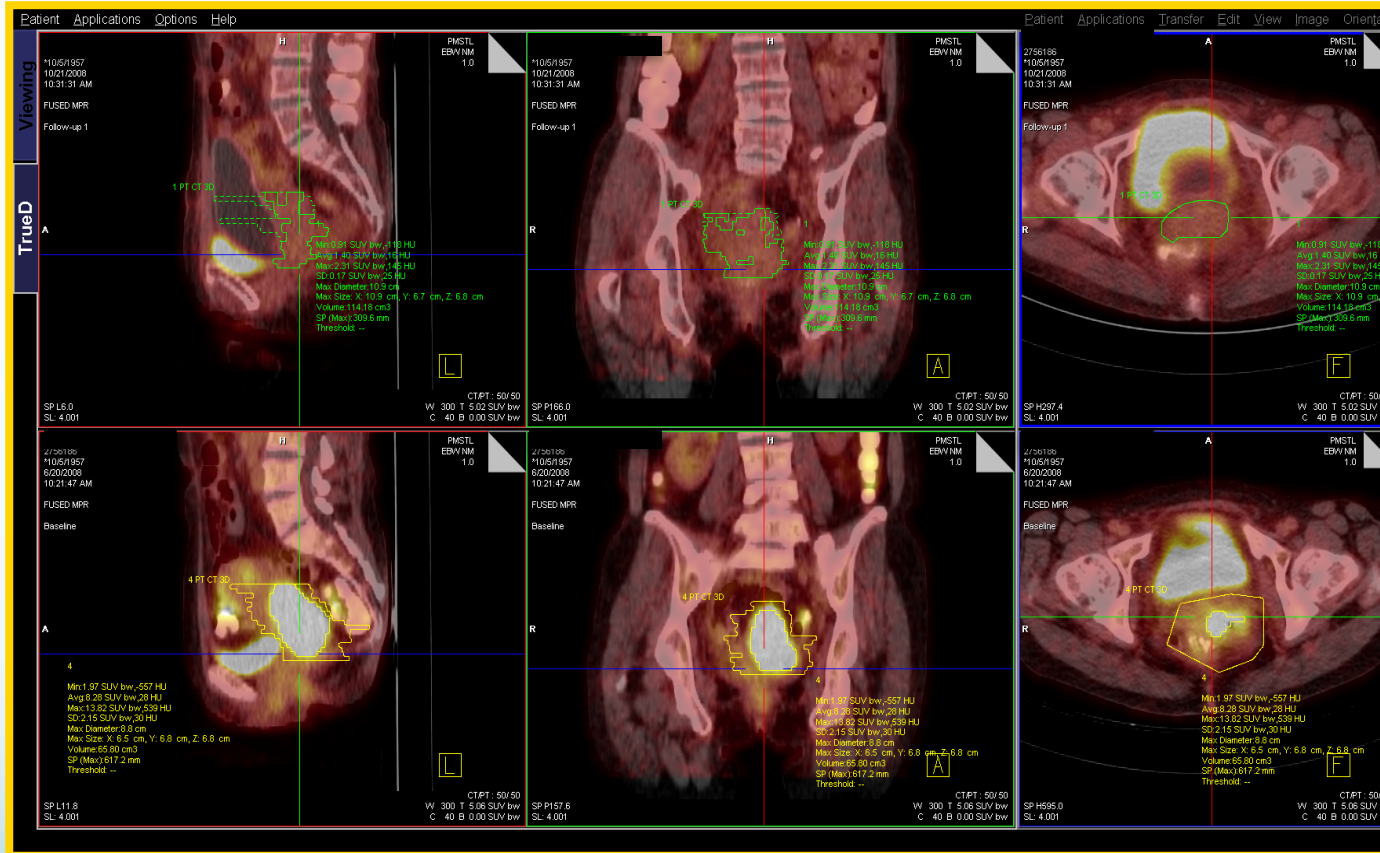


# Material & Methods:

## *Image analysis*



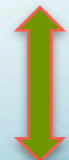
# Material & Methods: *Image analysis*



- ✓ SUVMax
- ✓ SUVMean
- ✓ Metabolic Volume (primary tumour)

- ✓ Ratio SUV Max
- ✓ Ratio SUV Mean

- ✓ SUVMax
- ✓ SUVMean
- ✓ Metabolic Volume (primary tumour)



- ✓ FIGO
- ✓ LN +
- ✓ Bulk

- ✓ OTT
- ✓ Age



# Results:

## *Recurrence (n=82, only prett PET)*

Significance for DFS: Median follow-up 19.6 months (2.4-71)

| Variable                  | Pre-RT Scan only<br>(N = 82) |        | Pre+ Post -RT Scan<br>(N = 48) |        |
|---------------------------|------------------------------|--------|--------------------------------|--------|
|                           | N                            | [%]    | N                              | [%]    |
| <b>FIGO status</b>        |                              |        |                                |        |
| IB                        | 10                           | [12.2] | 2                              | [4.2]  |
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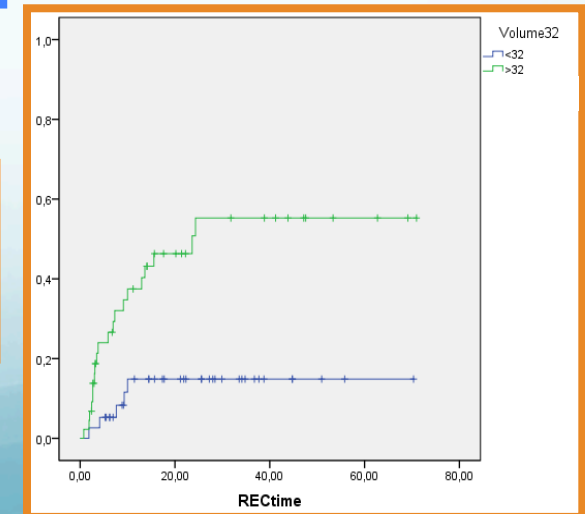
### Univariate analysis:

- FIGO stage [p=0.005],
- Bulk lesion [p=0.047]
- Pretreatment Metabolic Volume PETCT (MV-1) [p=0.004]

### Multivariate analysis:

- FIGO [p=0.018]
- Prett MV-1 [p=0.034]

Recurrence free survival plot for the subgroups of pts having a MV-1 over and under 32cc showed an highly significant difference of outcome (p=0.001)



## Results:

### *Clinical Response to treatment (n=48 pre +postt PET)*

- For the final analysis pts were grouped as “complete responders” versus “not complete responders”.



- **Significant difference** for OS [ $p < 0.001$ ] and for DFS [ $p = 0.005$ ] was found between cCR vs non-cCR
- At **univariate analysis**: significant correlation with the probability achieving a clinical complete response to treatment:
  - FIGO stage [ $p=0.03$ ]
  - Nodal involvement [ $p=0.04$ ]
  - post PET SUV max [ $p=0.03$ ]
  - Ratio of SUVMax (prePET/postPET) [ $p=0.03$ ]
- At **multivariate analysis** only FIGO [ $p=0.05$ ] and SUVMax2 [ $p=0.02$ ] remained significant when combined together.

## Conclusions:

We confirmed our hypothesis:

1. *Pretreatment* Metabolic volume (but not SUVmax) predict outcome (DFS) in cervix cancer
  2. Clinical response 2-3 months after treatment is a early surrogate of Disease Free Survival and Overall survival
  3. SUV ratio and SUV posttreatment is a better clinical response predictor then pretreatment SUVmax pretreatment
- Future prospects: Longer fup, Larger databes (higher n° events), External validation, Radiomics

## Acknowledgments:

Prof. Philippe Lambin  
Ludy Lutgens MD  
Ruud van Stiphout PhD

