PET and MRI in radiotherapy: A volumetric and dosimetric evaluation of target volume delineations and radiation treatment plans in gynaecological oncology.

Kelly Hunnego, May 2012

Dissertation Master Radiation Oncology in Europe
PET and MRI in radiotherapy: A volumetric and dosimetric evaluation of target volume delineations and radiation treatment plans in gynaecological oncology

Dissertation Master Radiation Oncology in Europe, Faculty of Health, Sports an Social work, Inholland University of Applied Sciences, Haarlem, the Netherlands

Author:
Kelly Hunnego
Haarlem, May 2012

Supervisors:
Emmy Lamers, MSc, Research Fellow Medical Technology
Iain Bruinvis, Ph. -D., Associate Lector Medical Technology
Inholland University of Applied Sciences, Haarlem, the Netherlands

Peter Koper, M.D., Ph. D.
Radiotherapy Centre West, The Hague

Tanja Stam, M.D.
Radiotherapy Centre West, The Hague

© 2012 K. Hunnego
Summary

The objectives of this study were to determine the benefits of using PET-and MRI-scan to the additional CT, in terms of delineation of target volumes and critical organs, and therefore also in the treatment planning.

8 patients with stage II-IV cervical, endometrium or vaginal cancer, according to the International Federation of Gynecology and Obstetrics guidelines, treated with IMRT between June 2011 and December 2011 at the Radiotherapy Centrum West, The Hague, were included. Patients with other gynaecological malignancies or palliative intent were excluded. Patients with contraindications such as pacemakers or poor renal function were also excluded. All patients underwent a PET-CT scan and MRI-scan, imaged supine in treatment position using a flat table top insert. To mark the top of the patient’s vagina, a tampon was inserted before PET/CT. No intravenously contrast was used.

Three physicians defined clinical target volumes (CTV) as well as organs at risk on respectively the CT, MRI-CT and PET-CT scan. All used GEC-ESTRO guidelines as well as the RCWEST medical protocol. Planning Target Volume (PTV) was defined as CTV-primary tumour (CTV$_{PR}$) plus CTV-lymph nodes (CTV$_{LN}$) with applied margins. To determine the correspondence between all CTV’s from respectively CT, CT-MRI and PET-CT scan, a Conformity Index (CI) and a Lesion Coverage Factor (CVF) were adapted. To determine the effect of using MRI-scan and PET-scan on treatment volume delineation, a paired t-test was adapted from SPSS.

An IMRT treatment plan was developed for all patients, based on target volumes and organs at risk, delineated on the CT-scan. The IMRT planning was performed using the Pinnacle Planning System version 8.0 m (Philips Healthcare). To study what the effects were on target volume coverage and dose to surrounding organs at risk, three patients were re-planned on respectively MRI-CT PTV and PET-CT PTV. Therefore the MRI and PET-studies were transferred to the treatment planning system. The two image studies were registered first automatically by grey scale and, if necessary, then adjusted manually by bony anatomy and iliac vessels. To evaluate dosimetric consequences of PET-scan and MRI-scan on radiation treatment plans, a CI was adapted.

In total, 66 datasets were delineated. Between patients there were major differences in volume, due to FIGO stage and positive detection of lymph nodes. For the patients with positive lymph nodes (38% of the patient group), large CTV$_{LN}$ were delineated (larger than 400 cc) on CT. Within this category of patients, large standard deviations with range 285-300 cc in mean volume were determined on both CT and PET-CT scans. Mean volumes of CTV$_{PR}$ are considerably less, compared to CTV$_{LN}$. Differences in CTV$_{PR}$ were also due to extent of the disease. Patients with large CTV$_{PR}$ (larger than 400 cc) had standard deviations that were proportional (larger than 135cc).
Then 32 treatment plans were created, based on CT data. When treatment planning was performed on CT delineations, an optimal coverage could be achieved for CT PTV$_{LN}$ and PTV$_{PR}$. MRI-CT and PET-CT PTV$_{LN}$ were analyzed in the same treatment planning; the CI was now respectively 0.93 and 1. Also for MRI-CT and PET-CT PTV$_{PR}$ the CI’s were respectively 0.95 and 0.96.

Three randomly chosen patients were re-planned on MRI-CT PTV and PET-CT PTV. During IMRT optimization these volumes were integrated into the objective list. Target coverage of MRI-CT PTV and PET-CT PTV now could be optimized easily. MRI-CT and PET-CT PTV$_{PR}$ and PTV$_{LN}$ were covered by 43.7Gy (95% of the prescription dose) with 99% of the volume and also the mean dose to organs at risk was slightly optimized.

In this study the number of patients was relatively small, more time and patients are needed to determine the consequences of using MRI and PET and therefore to define the exact CTV. Also fusion of different modalities is still influenced by differences in bladder and rectal filling, due to time gap between examinations. To use the benefits of both the MRI and PET-scan, the process of image fusion needs to be optimized.

No common guidelines are provided about how to work with MRI- and PET-scan in the treatment planning system. Regulations are needed to accept or reject PET and/or MRI data sets. For this paper it caused variations between participating physicians.

If, in the future, PET is combined with CT for radiotherapy purposes to define target volumes a Standard Uptake Value (SUV) value could optimize the delineation process. As discussed earlier, some of the delineation results are affected by bad image fusion. This resulted in slight rotations of the MRI-CT and PET-CT CTV and therefore to the PTV. For analyzing the treatment planning results this had a direct influence on the target coverage.

MRI shows positive results for mean CTV$_{LN}$ . Using the MRI combined with the CT-scan, mean CTV$_{LN}$ decreased for almost every patient. Based on these results, MRI shows a positive effect on CTV$_{LN}$ as well as for the standard deviations compared to CT only (p=0.041). To define CTV$_{PR}$ the use of MRI-CT scan has a slightly positive influence compared to CT-scan only. PET-CT seems to be most effective in decreasing CTV$_{PR}$ compared to CT (p= 0.022). If MRI and/or PET are used to define CTV$_{LN}$ a CTV$_{PR}$, treatment planning on these structures is recommended. Because of a different size and shape of target volumes on MRI-CT and PET-CT scan, dose coverage to the PTV can be increased and dose to organs at risk can be minimized.
Acknowledgements

I would like to express my gratitude to my supervisors, Emmy Lamers, Iain Bruinvis, Peter Koper and Tanja Stam, for the excellent guidance and support the past year. With their help and feedback my research and dissertation was made possible.

I would like to thank Dr. Monique Bloemers of the Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital for all her time and work, with her help she gave my dissertation that extra dimension.

I would like to thank Erik Kouwenhoven, Eric Franken and Edwin van der Wal for their help during my research for this dissertation. Of course I would like to thank all my colleagues of the Radiotherapy Centre West for their help and support the past year.

Finally, I would like to thank my partner and family, they were always supporting me and encouraging me when necessary.
# Contents

1. Introduction .................................................................................................................. 7

2. Materials and methods .................................................................................................... 8
   2.1 Patient characteristics ................................................................................................. 8
   2.2 FDG-PET/CT imaging ................................................................................................. 9
   2.3 MRI imaging .............................................................................................................. 10
   2.4 Treatment planning ................................................................................................... 10
      2.4.1 Procedure ........................................................................................................... 10
      2.4.2 Target volume contour delineation ....................................................................... 11
      2.4.3 Defining volumes organs at risk .......................................................................... 11
      2.4.4 Beam setup and IMRT parameters ....................................................................... 11
   2.5 Target volume delineation .......................................................................................... 12
   2.6 Statistical analysis .................................................................................................... 12

3. Results ............................................................................................................................ 14
   3.1 Results delineation study ............................................................................................ 14
      3.1.1 Effect MRI and PET on CTV lymph nodes ......................................................... 14
      3.1.2 Effect MRI and PET on CTV primary tumour ..................................................... 17
   3.2 DVH analysis part I ..................................................................................................... 19
      3.2.1 Target volume coverage....................................................................................... 19
      3.2.2 Dosimetric effects on organs at risk .................................................................... 20
   3.3 DVH analysis part II ................................................................................................... 21
      3.3.1 Target volume coverage ..................................................................................... 21
      3.3.2 Dosimetric effects on organs at risk ................................................................... 22

4. Discussion ....................................................................................................................... 23

5. Conclusion ....................................................................................................................... 25

6. References ....................................................................................................................... 26

7. Attachments ..................................................................................................................... 27
1. Introduction

The treatment of gynaecological malignancies has changed over time. In radiotherapy treatment there have been major improvements in treatment of gynecological malignancies. The use of intensity-modulated radiation therapy (IMRT) has been shown to help limiting dose to surrounding normal tissues and thereby decreasing toxicity [1]. Also the use of MRI for brachytherapy treatment planning has recently been investigated. MRI at the time of brachytherapy allows an accurate tumour delineation and dose optimization [2]. Recent publications have shown that Fluoro-Deoxy-Glucose Positron Emission Tomography (FDG-PET) plays an increasingly important role in radiotherapy, beyond staging and selection of patients [3]. Using FDG-PET-CT to define Gross Tumour Volume (GTV) for treatment planning purposes is relatively new for gynaecological tumours in radiotherapy treatment.

New diagnostic modalities including MRI and FDG-PET make it possible to visualize and define tumour sites more accurately in external beam therapy. Recent studies described the use of PET-scans and MRI-scans in cervical cancer in addition to defining the target volume. Grigsby et al. showed that cervical cancer and the use of PET and MRI for certain patient groups has a significant advantage [4]. However, the effect of using PET and MRI for gynaecological malignancies on delineation variations between physicians has not been determined. Neither have the consequences of these results on treatment planning been reported. The assumption is that use of extra modalities will have a positive effect on treatment planning; by achieving better target volume coverage and decreased toxicity of surrounding organs at risk.

The objectives of this study are therefore to determine the benefits of using PET- and MRI-scans as addition to CT-scans, in terms of delineation of target volumes and organs at risk and thus also in treatment planning.

Chapter 2 describes the study design, use of PET-CT and MRI, as well as the delineation procedure and the statistical analysis. In chapter 3 the results of the delineation study and treatment planning study are presented. Chapter 4 and 5 contains the discussion and conclusion derived from results in chapter 3. References and attachments can be found in Chapters 6 and 7 respectively.
2. Materials and methods

2.1 Patient characteristics

Patients with stage II-IV cervical, endometrium or vaginal cancer, according to the International Federation of Gynecology and Obstetrics guidelines, treated with IMRT between June 2011 and December 2011 at the Radiotherapy Centrum West, The Hague, were included. Patients with other gynaecological malignancies or palliative intent were excluded. Patients with contraindications such as pacemakers or poor renal function were also excluded.

Between June 2011 and November 2011, 8 patients were selected for the study and underwent PET-CT and MRI simulations. Characteristics of patients and tumour-related factors are presented in Table 1. The patient age ranged from 46 to 79 years, mean age 60 years. Six patients were diagnosed with cervical cancer; two patients were diagnosed with vagina carcinoma. Three patients (38%) had lymph nodes detected on the PET-CT scan; one of them also had para-aortic nodal involvement. In five patients (62%) no iliac nodes were clinically detected.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Level</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td></td>
<td>8 (100)</td>
</tr>
<tr>
<td>Age</td>
<td>Mean (range)</td>
<td>60 (46-79)</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Cervix carcinoma</td>
<td>6 (75%)</td>
</tr>
<tr>
<td></td>
<td>Vaginal carcinoma</td>
<td>2 (25%)</td>
</tr>
<tr>
<td>FIGO stage</td>
<td>I</td>
<td>3 (37%)</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>2 (25%)</td>
</tr>
<tr>
<td></td>
<td>IIIa</td>
<td>3 (38%)</td>
</tr>
<tr>
<td></td>
<td>IIIb</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>0</td>
</tr>
<tr>
<td>Histology</td>
<td>Squamous cell carcinoma</td>
<td>8 (100%)</td>
</tr>
<tr>
<td></td>
<td>Adenocarcinoma</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>0</td>
</tr>
<tr>
<td>Nodal involvement</td>
<td>Common iliac only</td>
<td>2 (25%)</td>
</tr>
<tr>
<td></td>
<td>Lower para-aortic with/without common iliac nodes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Upper para-aortic with/without iliac/lower para-aortic lymph nodes</td>
<td>1 (12.5%)</td>
</tr>
</tbody>
</table>

Table 1: Patient and tumour characteristics
Pretreatment workup included histology, gynaecologic pelvic examination, and biopsy, computed tomography and complete blood count. The clinical stage and plan of treatment were determined in a multidisciplinary conference. MRI- and PET-scans in combination with CT scans were manufactured for radiotherapy treatment planning purposes. MRI is already used next to the additional CT in order to define GTV and is most commonly used to determine tumor extension in the parametrium. The PET-scan was used to determine positive common iliac and para-aortic nodal involvement but also for comparative purposes in delineation of treatment volumes.

All patients were treated with a combination of external beam therapy with IMRT, internal high dose rate (HDR) brachytherapy and concurrent weekly chemotherapy with Cisplatin. In external beam therapy the abdominal-pelvic fields received a dose of 46 Gy in 23 fractions, in brachytherapy a total dose of respectively 18-21Gy in 3 fractions was received [5]. Dose and fractionation pattern were related to extent of the disease and related expected toxicity during treatment.

2.2 FDG-PET Imaging

Recent publications emphasize the increasing role of PET-CT scans in the diagnosis and treatment of gynaecological cancers [6]. Recently PET-scans have been shown to be a highly sensitive method to determine lymph node status. To integrate PET-CT scans into the radiotherapy treatment planning process represents a challenging issue [7].

Patients were intravenously administered (2MBq/kg) 18F-fluorodeoxyglucose (FDG) and, 75 minutes later, underwent a PET-CT scan. Both PET and CT images were produced with a Siemens Biograph 64 Truepoint PET-CT scanner at the radiology department of the Haga Hospital, The Hague. Patients were imaged supine in treatment position using a flat table top insert. To mark the top of the patient’s vagina, a tampon was inserted. No intravenously contrast was used in this trial. For the CT component of the PET-CT scan, the scan parameters were 3 mm thick CT images and the scan starting at the orbital cavity up to the proximal femur. For the PET component, series of five to six bed positions were used over the same anatomical extent as for the CT-scan. For each bed position a scan time of 4 minutes was maintained.

Immediately after the PET scan, a second CT scan was acquired of the patients using similar parameters as for the first CT-scan. The second CT-scan was used for treatment planning and dose calculations purposes. Figure 1 shows a PET image, CT image en registered images of PET- and CT-scans. The entire contents of the PET-CT protocol can be found in attachment 7.1.
2.3 MRI imaging

Magnetic Resonance Imaging (MRI) has been shown to be the best exam to assess tumour in cervix cancer, especially to detect tumour extension in the parametrium[8]. Because of its superior soft-tissue contrast (figure 2), MRI has also benefits in defining and delineation of target volumes in radiotherapy treatment [9].

All anatomic MRI images in this study were produced with the 1.5 Tesla Siemens Magnetom Symphony syngo MR A35 at the radiology department of the Medical Centre Haaglanden, The Hague. All patients were scanned in treatment position using a flat table top insert. A set of multi-slice, T2-weighted Turbo Spin Echo (TSE) and Gradient echo images, in both axial and sagittal orientations, were acquired with a field of view of 35 cm, excitation time of 98 ms, relaxation time of 3400 ms, turbo factor of 15 and slice thickness of 3 and 4 mm.

A number of coils were used to increase the image quality for radiotherapy treatment simulation. The entire contents of the MRI protocol can be found in attachment 7.2

2.4 Treatment planning

2.4.1 Procedure

For all patients an IMRT treatment plan was designed, based on target volumes and organs at risk delineated on a CT-scan. To study what the effects of using other image modalities are on target volume coverage and dose to surrounding organs at risk, three patients were re-planned based on target volumes and organs at risk delineated on respectively MRI-CT and PET-CT scans. Therefore MRI and PET studies were transferred to the treatment planning system. The two image studies were registered first automatically by grey scale values and, if necessary, then adjusted manually using bony anatomy and iliac vessels as a guidance.

The IMRT treatment planning was performed using the Pinnacle Planning System version 8.0 m (Philips Healthcare). In order to compare treatment plans later on in this study during DVH analysis, all patients were planned with a prescription for the combined PTV lymph nodes and PTV cervix/vagina of 46 Gy in fractions of 2 Gy.

Treatment planning was performed by four different radiation technologists using the RCWEST IMRT planning protocol for gynaecological malignancies (attachment 7.4). During the treatment planning procedure, optimization of the IMRT plans was repeated until 99% of the PTV volume was covered by 95% of the prescribed dose. In accordance with ICRU...
reports, more than 1% of the PTV volume receiving more than 107% of the prescription dose was not accepted [10].

2.4.2. Target volume contour delineation

Target volume was defined on the CT-scan, according to the RCWEST protocol, as CTV primary tumour (CTV\textsubscript{PR}) plus CTV lymph nodes (CTV\textsubscript{LN}) with applied margins. For each patient the extent of CTV\textsubscript{PR} was related to FIGO stage. For each patient CTV\textsubscript{LN} were defined as lymph nodes following the internal and external iliac arteries up to promotorium level. If lymph nodes were detected on CT, the highest attached lymph nodes were also delineated. The CTV-PTV margin for CTV\textsubscript{PR} that was applied for this patient group was 1.0 cm in lateral, 1.5 cm in cranial-caudal and 2.0 cm in dorso-ventral direction. The CTV-PTV margin that was used for CTV\textsubscript{LN} was 0.5 cm in each direction (attachment 7.3).

2.4.3 Defining volumes organs at risk

For gynaecological patients a number of organs at risk were delineated by radiation technologists and checked by a physician. For treatment planning of gynaecological malignancies, anal canal, rectum, bladder and bowel area were defined to be used in the IMRT optimization.

The anal canal was defined as the first 3 cm’s of the rectal canal. The rectum was defined as the part cranial from the anal canal up to the sigmoid (figure 3). The bladder was also delineated. Finally the “bowel area” was delineated, defined as every possible bowel structure up to 2 cm’s cranial from the PTV (figure 3).

![Figure 3: On the left, Anal canal (purple), rectum (brown), right bowel area (olive)](image)

2.4.4 Beam setup and IMRT parameters

For all patients a treatment planning was created using the RCWEST planning protocol for gynaecological patients (attachment 7.4). For this planning technique an equally spaced, seven field beam setup was used with 10MV photon beams. To minimize tongue and groove effect, a collimation rotation of 6 degrees in every beam was applied in every beam.

A maximum number of 35 segments was used with a minimum segment size of 25 cm\textsuperscript{2}. The minimum number of monitor units was set to 4 MU for each segment.
2.4.5 Dose constraints and objectives

Dose-volume constraints for normal tissues included: mean dose of bladder as low as possible, mean dose of anus less than 45Gy, maximum dose of bowel area as low as possible, mean dose of rectum less than 45Gy.

The objectives list used for gynaecological malignancies contains objectives for the target volume and a number of “auxiliary structures” to achieve high dose gradients around the PTV. For the target volume min DVH and Uniform dose objectives were used to achieve a dose of 43.7Gy (95% prescription dose) in 99% of the volume. A ring around the PTV was created with a max Dose constraint to achieve high dose gradients (figure 4). For all organs at risk, auxiliary structures were created without overlap with the PTV and the PTV ring (figure 4). Objectives with max EUD were used for these auxiliary structures to decrease the mean dose and the maximum dose to organs at risk. To minimize hotspots to the surrounding tissues, a body outline excluding the PTV and the PTV ring was created.

Figure 4: screenshot of ring structure (orange) and auxiliary structures for rectum (maroon) and bowel area (turquoise)

All objectives used in the optimization procedure can be found in the planning protocol in annex 7.4.

2.5 Target volume delineation procedure

Three physicians, two of the radiotherapy department of the Radiotherapy Centre West and one of the Netherlands Cancer Institute- Antoni van Leeuwenhoek Hospital, delineated contours to determine target volumes as well as organs at risk on respectively the CT, MRI-CT and PET-CT scans. All physicians used GEC-ESTRO guidelines as well as the RCWEST medical protocol for gynaecological malignancies in the delineation process (attachment 7.3) [2, 4]. The results of these delineations were analyzed by determining the effect of using different modalities for each physician as well as conformity between the participating physicians. The effect of using CT, CT-PET and CT-MRI scans on target volume delineation was determined for each physician by calculating a standard deviation, a conformity index and a paired t-test. The exact statistical analysis is presented in subsection 2.6.
2.6 Statistical analysis

To determine what the volumetric consequences are of using extra imaging modalities on the delineation of the target volume and normal tissues, a volumetric analysis has been performed. To compare the correspondence between CTV delineations on respectively CT, CT-MRI and PET-CT scans a Conformity Index (CI) and a Lesion Coverage Factor (CVF) were adapted. The following CI was used to determine the relative concordance between MRI-CT and PET-CT CTV [4]:

\[
\text{Conformity Index} = \frac{\text{CTV MRI}_{\text{Vol}}}{\text{CTV PET}_{\text{Vol}}}
\]

The lesion coverage factor (CVF) was used to determine the percentage of overlap between volumes [4].

\[
\text{CVF} = \frac{\text{Overlap between MRI-CTV}_{\text{vol}} and FDG PET-CTV}_{\text{vol}}}{\text{FDG PET-CTV}_{\text{vol}}}
\]

To determine the effect of using MRI- and PET-scans on PTV delineation, a paired t-test was adapted from SPSS. A value of \( p < 0.05 \) was set as the threshold for significance for all study outcomes.

To analyze (target) delineation variations between the participating physicians a standard deviation based on target volumes (cm\(^3\)) was calculated. With this standard deviation the effects of using MRI en PET images on these variations were determined.

To evaluate the dosimetric consequences of MRI-and PET-scans on radiation treatment plans, the following irradiation conformity index was used [12, 13]:

\[
\text{Conformity index}_{\text{RTOG}} = \frac{V_{\text{RI}}}{\text{TV}}
\]

\( V_{\text{RI}} \) = reference isodose volume (cc), defined as 95% of the prescription dose

\( \text{TV} \) = planning target volume(cc).

The values of each of these parameters have been defined for treatment plans based on respectively CT, MRI-CT and PET-CT delineations to determine the quality of irradiation. The effects on surrounding normal tissues and organs at risk will be defined by analyzing dose volume histograms with dose constraints outlined in subsection 2.4.5.
3. Results

In total, 66 datasets including target volumes and organs of risk were delineated. Variations between participating physicians as well as the effect of using extra modalities on these variations are presented in subsection 3.1. With this data, over 38 treatment plans were created by four different radiation technologists. The results of this planning study are presented in subsection 3.2 and 3.3.

For the purpose of accurate (statistical) analysis, all results were analyzed for CTV’s of lymph nodes as well as for CTV’s for primary tumours.

3.1 Results delineation study and statistical analysis

Because only 8 patients were included in this study, data could not be assumed to be normally distributed. To verify if the used data was approximating a normal distribution, the Kolmogorov-Smirnov-test was performed in SPSS software. Test results showed the data was not significant for lymph nodes and primary tumours. This assumed the data was normally distributed. Results are shown in attachments 7.5a and b.

3.1.1 Effect of MRI- and PET-scans on CTV lymph nodes (CTV\textsubscript{LN})

Based on 8 patients, the mean CTV\textsubscript{LN} on CT was 327 cc, with a range of 160-513 cc and a standard deviation of 135 cc. The mean MRI-CT CTV\textsubscript{LN} was 206 cc, with a range of 72-359 cc and a standard deviation of 138 cc, while PET-CT CTV\textsubscript{LN} 336 cc with range 160-508 cc, and standard deviation of 128 cc (Figure 5).

![Figure 5: Mean volumes CTV\textsubscript{LN}](image)

Between patients there were major differences in volume, ranging between 160-513 cc, due to FIGO stage and positive detection of lymph nodes (Table 2). Patient 1, 5 and 7 were detected with positive lymph nodes (38% of the patient group). Two patients had positive lymph nodes in respectively para-aortal and mesenteric region and small pelvis region. This resulted in large CTV\textsubscript{LN} volumes (larger than 400 cc) and large standard deviations with a range of 285-300 cc. For patients with no lymph nodes detected (62% of the patient group),
relatively small CTV\textsubscript{LN} volumes (smaller than 300 cc) were defined with small standard deviations with a range of 44-118 cc.

<table>
<thead>
<tr>
<th>Patient number</th>
<th>CT CTV\textsubscript{LN} (cc)</th>
<th>MRI-CT CTV\textsubscript{LN} (cc)</th>
<th>PET-CT CTV\textsubscript{LN} (cc)</th>
<th>Conformity index</th>
<th>Lesion coverage factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>513</td>
<td>359</td>
<td>508</td>
<td>0.7</td>
<td>0.3</td>
</tr>
<tr>
<td>2</td>
<td>388</td>
<td>0</td>
<td>392</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>335</td>
<td>255</td>
<td>340</td>
<td>0.8</td>
<td>0.4</td>
</tr>
<tr>
<td>4</td>
<td>160</td>
<td>274</td>
<td>160</td>
<td>1.7</td>
<td>0.8</td>
</tr>
<tr>
<td>5</td>
<td>452</td>
<td>236</td>
<td>518</td>
<td>0.5</td>
<td>0.3</td>
</tr>
<tr>
<td>6</td>
<td>193</td>
<td>78</td>
<td>193</td>
<td>0.4</td>
<td>0.3</td>
</tr>
<tr>
<td>7</td>
<td>272</td>
<td>166</td>
<td>272</td>
<td>0.6</td>
<td>0.5</td>
</tr>
<tr>
<td>8</td>
<td>305</td>
<td>72</td>
<td>305</td>
<td>0.2</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 2: Patient volume measurements of CTV\textsubscript{LN} volumes

If the three groups (CT, MRI-CT and PET-CT) are compared by volumes of CTV\textsubscript{LN}, no difference between volumes on CT and PET-CT scans could be determined. 62% of the patients were not detected with positive lymph nodes. If no lymph nodes were detected on FDG-PET, no activity and therefore no contours were visible on these images. Nevertheless, iliac lymph nodes were taken into the radiotherapy treatment plan. Physicians defined a CTV\textsubscript{LN} as described in the medical protocol (attachment 7.4) and used the additional CT to define CTV\textsubscript{LN}.

The use of MRI-CT will decrease the range of CTV\textsubscript{LN} volumes [9, 14,15]. Because MRI-images have an excellent image quality, MRI shows positive results for mean CTV\textsubscript{LN} (Table 2, Figure 6). Using the MRI-scan combined with additional CT-scan, mean volumes decreased for almost every patient. In 6 out of 7 seven patients mean volumes ranged from 72-274 cc due to extent of disease. With exception of patient 1, the standard deviations ranged between 34 and 133.

Based on these results, the use of the MRI-scan to the additional CT-scan have shown positive effects on the mean CTV volumes as well as for the standard deviations, compared to volumes and standard deviations based on CT-scan only (p=0.041). Mean conformity index (CI) of MR-CT and PET-CT CTV\textsubscript{LN} was 0.7 ± 0.5 with a mean lesion coverage factor (CVF) of 0.4 ± 0.2.
Because the group of patients is relatively small and there were only three physicians to delineate all datasets, we assume that the result also can be affected by the physician. Therefore the research data was also analyzed by physician. Results are shown in Figure 7.

Results by physician show no major differences between CT and PET-CT scans. Because most of the patients (62%) were not detected with positive lymph nodes, CT images were used to define CTVLN. This resulted in hardly any differences in mean CTVLN on CT-scan and PET-CT scan.

Results in Figure 7 show major difference in MRI-CT CTVLN between physicians. Physician 1 and 2 clearly used MRI-images in all cases to define CTVLN, compared to physician 3. Volumes decreased almost by 50% for physician 1 and 2. Results for physician 3 demonstrate almost no difference between CT, MRI-CT and PET-CT scans.
3.1.2 Effect of MRI- and PET-scan on CTV primary tumour (CTV\textsubscript{PR})

Results for CTV\textsubscript{PR} were 240 cc on CT, with a range of 125-442 cc and a mean standard deviation of 59 cc. The mean MRI-CT CTV\textsubscript{PR} was 186 cc, with a range of 96-401 cc and a mean standard deviation of 52 cc, while the mean PET-CT CTV\textsubscript{PR} was 153 cc with a range of 68-227 cc, and a mean standard deviation of 81 cc (Figure 8).

![Figure 8: Mean CTV\textsubscript{PR}](image)

The differences between patients were due to FIGO stage and therefore extent of the disease (Table 3, Figure 8). Patient 1 was diagnosed with cervical cancer FIGO stage IIIa, with an invasion into the parametric region, bladder and part of the rectum. Therefore the CT CTV\textsubscript{PR} is clearly larger compared to the CTV\textsubscript{PR} of other patients.

Patient 5 and 6 were diagnosed with vaginal cancer; the other patients were diagnosed with cervical cancer and a FIGO stage II-IIlb. Patients with a large CTV\textsubscript{PR} (larger than 400 cc) demonstrated a large standard deviation (larger than 135cc). The MRI-CT shows only a decrease in CTV\textsubscript{PR} volume for patient 1, 6, 7 and 8; for the other patients MRI-CT increases CTV\textsubscript{PR}. Because patient 2 not underwent MRI scan due to physiological problems, no results can be presented. PET-CT seems most effective in decreasing CTV\textsubscript{PR} for 7 patients. The volumes of CTV\textsubscript{PR} are here ranging from 68-227 cc compared to 125-442 cc for the additional CT only (p= 0.022) (Figure 9).

The mean conformity index (CI) for CTV\textsubscript{PR} was $1.4 \pm 0.4$ with a mean lesion coverage factor (CVF) of $0.3 \pm 0.2$. Compared to CI for CTV\textsubscript{LN} (CI= $0.7 \pm 0.5$), delineated volumes for CTV\textsubscript{PR} demonstrate more correspondence on MRI-CT and PET-CT.
Table 3: Patient volume measurements of CTV

<table>
<thead>
<tr>
<th>Patient number</th>
<th>CT CTV_{PR} (cc)</th>
<th>MRI-CT CTV_{PR} (cc)</th>
<th>PET-CT CTV_{PR} (cc)</th>
<th>Conformity index</th>
<th>Lesion coverage factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>442</td>
<td>237</td>
<td>207</td>
<td>1.1</td>
<td>0.4</td>
</tr>
<tr>
<td>2</td>
<td>125</td>
<td>-</td>
<td>161</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>169</td>
<td>185</td>
<td>164</td>
<td>1.1</td>
<td>0.1</td>
</tr>
<tr>
<td>4</td>
<td>370</td>
<td>401</td>
<td>227</td>
<td>1.8</td>
<td>0.6</td>
</tr>
<tr>
<td>5</td>
<td>213</td>
<td>237</td>
<td>154</td>
<td>1.5</td>
<td>0.2</td>
</tr>
<tr>
<td>6</td>
<td>144</td>
<td>132</td>
<td>68</td>
<td>1.9</td>
<td>0.1</td>
</tr>
<tr>
<td>7</td>
<td>257</td>
<td>199</td>
<td>126</td>
<td>1.6</td>
<td>0.6</td>
</tr>
<tr>
<td>8</td>
<td>200</td>
<td>96</td>
<td>116</td>
<td>0.8</td>
<td>1.1</td>
</tr>
</tbody>
</table>

Results by physician are presented in Figure 10. Also for defining CTV_{PR} hardly any difference can be determined between CT, MRI-CT and PET-CT scans by physician 3.

Physician 1 and 2 show a decrease in CTV_{PR} by MRI-CT and PET-CT scans. If the CTV_{PR} from CT and PET-CT scans are compared, mean volumes of the PET-CT scans decreased by almost 50%! The use of PET-CT resulted in a reduction of respectively 127 cc (SD= 118 cc) and 108 cc (SD=62cc) for physician 1 and 2.
3.2 DVH analysis part I

In total, 32 treatment plans were created by four different radiation technologists on CT data. For every patient, three CT datasets from different physicians were available, the CT dataset that was used for treatment planning was chosen at random. The following results represent the evaluation based on CT as well as on MRI-CT and PET-CT scans. All results were dosimetric evaluated by target coverage and dose to surrounding organs at risk.

3.2.1. Target volume coverage

Because treatment planning was performed on a CT-scan, $D_{99\%}$ of 43.7 Gy (95% of the prescription dose) was achieved for the $PTV_{PR}$ as well as the $PTV_{LN}$ for all patients. Mean target coverage at 43.7 Gy of $PTV_{LN}$ by MRI-CT and PET-CT was respectively 94% and 99% (Figure 3). Mean CI for $PTV_{LN}$ by MRI-CT is 0.93 ±0.07, by PET-CT this is 1.0±0.01.

No loss of any target coverage of $PTV_{LN}$ by PET-CT could be determined, compared to coverage of the $PTV_{LN}$ by MRI-CT (Figure 11).
Results for MRI-CT and PET-CT PTVPR were covered with 43.7Gy by respectively 95% and 96% (Figure 12). For MRI-CT PTVPR the mean CI was now 0.95 ±0.07, for PET-CT PTVPR this was 0.96±0.09.

3.2.2. Dosimetric effects on organs at risk

Because of the poor image quality on the PET-scan, organs at risk on the PET-CT dataset are always delineated on CT. Therefore, to evaluate the effects on organs at risk, only CT and MRI-CT scans were analyzed (Figure 13).

Figure 13 shows hardly any differences between CT and MRI-CT scan in terms of mean dose (Dmean) to the anus (Dmean = 32Gy vs. 31.4Gy) and bladder (Dmean = 39Gy vs. 39.4Gy). Nevertheless, for both the rectum (Dmean = 43 vs. 39.5) and the bowel area (Dmean = 23Gy vs. 30.1Gy) a small difference was determined between CT and MRI-CT. Because the bowel area volumes are always relative, no statements can be made for this “critical organ” in terms of Dmean.
No major differences were determined between CT and MRI-CT in terms maximum dose ($D_{\text{max}}$) to the bladder ($D_{\text{max}}=$ respectively 49Gy, 47.8Gy) and bowel area ($D_{\text{max}}=$ respectively 49Gy, 48.8Gy). On both CT and MRI-CT an overlap of all organs at risk with the PTV explain why no major differences in $D_{\text{mean}}$ and $D_{\text{max}}$ can be determined.

### 3.3 DVH analysis part II

In order to evaluate the dosimetric consequences for dose coverage and dose to surrounding tissues if treatment planning was performed on PTV by MRI-CT and PET-CT scans, 3 randomly chosen patients were re-planned on the MRI-CT and PET-CT scan.

#### 3.3.1. Target volume coverage

After treatment planning was performed on MRI-CT and PET-CT datasets, target coverage was according to ICRU guidelines (*Figure 14 and 15*). $PTV_{PR}$ and $PTV_{LN}$ on MRI-CT now reached minimum target coverage ($V_{43.7Gy}$) of 99%. $PTV_{PR}$ and $PTV_{LN}$ based on PET-CT also reached minimum target coverage ($V_{43.7Gy}$) of 99%.

![Coverage PTV<sub>LN</sub>](image1)

*Figure 14: Coverage of $PTV_{LN}$ on respectively CT, MRI-CT and PET-CT scans*

![Coverage PTV<sub>PR</sub>](image2)

*Figure 15: Coverage of $PTV_{PR}$ on respectively CT, MRI-CT and PET-CT scans*
3.3.2 Dosimetric effects to organs at risk

In subsection 3.3.1, results showed better dose coverage for PTV_{LN} as well as for PTV_{PR}. Compared to results in subsection 3.2.2, the treatment planning system can now be forced during optimization to make higher dose gradients around the MRI-CT PTV and PET-CT PTV. This has a minimum effect on surrounding organs at risk and normal tissues. The results for organs at risk in terms of mean dose are presented in Figure 16.

Figure 16: Mean dose to organs at risk compared for CT, MRI-CT and PET-CT scans

In terms of $D_{\text{mean}}$ to organs at risk, the PET-CT scan seems to be slightly better than MRI-CT scan for the anus ($D_{\text{mean}} = 5\text{Gy}$ vs. $7\text{Gy}$), the bladder ($D_{\text{mean}} = 41\text{Gy}$ vs. $37\text{Gy}$) and the rectum ($D_{\text{mean}} = 42\text{Gy}$ vs. $38\text{Gy}$). Because the bowel area volumes are always relative, no statements can be made for this “critical organ” in terms of $D_{\text{mean}}$.

No major differences were determined between CT, MRI-CT and PET-CT scans in terms of $D_{\text{max}}$ to the bladder ($D_{\text{max}}$ respectively $49\text{Gy}$, $48.6\text{Gy}$ and $48.6\text{Gy}$) and bowel area ($D_{\text{max}}$ respectively $49\text{Gy}$, $48.6\text{Gy}$ and $48.4\text{Gy}$).
4. Discussion

The number of patients in this study is relatively small to determine accurate results with respect to delineation of the CTV as well as for the treatment planning. More time and patients are needed to determine the consequences of using MRI and PET to define the exact CTV for gynaecological malignancies.

In this study, besides patients diagnosed with cervical cancer also patients with vagina carcinoma were included in the study. To determine possible differences by tumour sites it is also necessary to include more patients diagnosed with other gynaecological malignancies besides cervical cancer.

Because both MRI and PET are not common used as registered images to CT, physicians used both modalities to their own conscience. This explains variations between physicians in mean volume for CTV\textsubscript{LN} as well as CTV\textsubscript{PR} on MRI-CT scan and PET-CT scan. On MRI-CT, a large decrease in mean volume is determined for physician 1 and 2. Physician 3 only used MRI to define CTV when image fusion was performed accurately. For some patients image fusion could not be performed well due to large variations in bladder and rectal filling. Because of this reason, physician 3 ignored the MRI database en delineated the CTV for some patients on CT only. Therefore results seems to be dependent by physician. To evaluate the use of both modalities in the planning system it is important all physicians use the extra information in the same way. Guidelines to use both MRI and PET in the delineation process could be helpful to optimize the effect of both modalities for this patient group.

Image fusion between different modalities is an important factor of uncertainty. A difference in bladder and rectal filling, due to the time gap between both examinations, affects accurate registration. Especially for MRI and CT and in some cases for PET-CT as well. In this study this resulted, for some of the patients, in slight rotations of the MRI-CT and PET-CT CTV and therefore to the PTV. The results in this study are, in some cases, affected because of bad image fusion. To use the benefits of both MRI scan and PET scan, the process of image fusion needs to be optimized. As described earlier by Ma et al., 2011, more research is necessary and better equipment needs to be developed to minimize differences between scans [4].

PET images show metabolic activity with a poor image quality, because of this property only contours of tumour activity can be determined. In combination with CT this is useful, not only to detect positive lymph nodes, but also to define tumour tissue. If this tool will be used in the future to define primary tumour tissue, a Standard Uptake Value (SUV) as well as standard window level settings for gynecological tumours is required. This, to optimize the quality of the delineation process and therefore decrease variations in defining CTV between physicians. Much literature is already available about the use of SUV in gynaecological malignancies but this is only for diagnostic purposes, not for radiotherapy treatment.
purposes [16]. More research about this feature for radiotherapy purposes is necessary to help optimize the delineation process.

The results with respect to the CI of $CTV_{PR}$ and $CTV_{LN}$ were based on the mean volumes of three physicians. Since there were large variations between the CTV’s of the physicians on MRI-CT and PET-CT scans, the CI of both $CTV_{PR}$ and $CTV_{LN}$ could be more accurate if they are calculated by physician. More conformity between physicians by using SUV values and delineation guidelines for MRI-CT and PET-CT in the future, could also be helpful to calculate more accurate values for CI for $CTV_{PR}$ and $CTV_{LN}$.

The CVF for both $CTV_{PR}$ and $CTV_{LN}$ was calculated by determining the overlap of target volumes between MRI and PET. The low CVF for both $CTV_{PR}$ and $CTV_{LN}$ could be assigned by the poor quality of image fusion for some patients, due to major differences in bladder and rectal filling. As discussed earlier, this resulted in rotations and slightly different positions of $CTV_{LN}$ and $CTV_{PR}$ on MRI-CT and PET-CT and therefore in a loss of the CVF.

During part I of the treatment planning study, results were analyzed by comparing target coverage of PTV on respectively CT, MRI-CT and PET-CT scans. The treatment planning was performed on target volumes and organs at risk, defined on the CT-scan. As discussed earlier, some of the delineation results are affected by bad image fusion. This resulted in slight rotations of the MRI-CT and PET-CT CTV’s and therefore also to the PTV. For analyzing the treatment planning results this also had consequences. Rotations of MRI-CT and PET-CT CTV’s had a direct influence on the target coverage results described in subsection 3.2.1. Target coverage of $V_{43.7Gy}$ by 99% of the volume for MRI-CT PTV was not optimal. If this was due to bad image fusion or by more accurate target volumes could not be concluded from this study.
5. Conclusion

If MRI images are combined with CT images, the mean CTV’s of lymph nodes will decrease. Therefore MRI shows a positive effect on mean CTV\textsubscript{LN} (p = 0.041). With the use of MRI images to the additional CT images also mean standard deviations of CTV\textsubscript{LN} will decrease, this means that lymph nodes can be defined more accurately.

If FDG-PET detects positive lymph nodes, metabolic activity is visible on these images. Combined with CT images, it will be a useful tool to define CTV\textsubscript{LN} for radiotherapy purposes. If no lymph nodes are detected, no contours are visible on FDG-PET images, therefore CT images can be used to define a CTV\textsubscript{LN} according to a medical protocol.

The use of MRI images to the additional CT has, in some cases, a slightly positive influence on the CTV of primary tumours. Nevertheless, the combination PET-CT seems to be most effective in decreasing mean CTV of the primary tumour, when compared to volumes based on only CT images. (p=0.022).

When MRI images and/or PET images are used to define primary tumours and lymph nodes for gynaecological malignancies, treatment planning on these structures is highly recommended. Because of a different size and shape of the target volumes on the MRI-CT and PET-CT scan, dose coverage to the PTV can be increased and mean dose to the organs at risk can be minimized. No major differences can be determined between CT, MRI-CT and PET-CT scan in terms of maximum dose to the bladder and bowel area. This is because of a standard overlap of the bladder, the rectum, the anus and the bowel area with the PTV, due to the large margin recipe used for gynaecological malignancies.
6 References


### Attachments

#### 7.1 PET-CT protocol

**HagaZiekenhuis**

---

**PET-CT Gynaecologie**

**Page**: 1

**Radiotherapie**

Auteur: KH

**28-12-11**

---

**Documentinformatie**

- **Documentnummer:**
- **Beheer:**
- **Plaats in DKS:**

**Toepasbaarheid**

Dit CT protocol is toepasbaar op de volgende tumorsites of tumorgroepen zoals die worden genoemd in het kwaliteitsstijemystem:

1. Gynaecologie

**Hulpmiddelen**

- **2 K:** Hoofdkussens
- **RBS:** Rode beensteun
- **Contrast:** géén IV contrast
- **Tampon:** Alleen bij gynaecologie als marker vaginatop
- **Blazinstructie:** Volle blaas

**Gegevens PET**

- **Radiofarmacon:** $^{18}$FDG- fluorodeoxyglucose
- **Aantal bedposities:** 5/6, afhankelijk van scanlengte
- **4 minuten per bedpositie**
- **Dosis patiënt:** 2MBq/kg

**Patiënt positionering**

- **Head First**
- **Gynaecologie:** Supine, 2K, RBS, voor positionering tampon inbrengen
PET- CT Gynaecologie

- Plaatsing tattoo's

Gynaecologie:

Scangebied CT en PET:

1. Gynaecologie: Buitenste gehoorgang- halverwege femur
7.2 MRI protocol

SIEMENS MAGNETOM Symphony syngo MR A35

Scan Time: 0:14  Voxel size: 3.11×1.6×10.0 [mm]  Rel. SNR: 1.00  SIEMENS: gre

<table>
<thead>
<tr>
<th>Routine</th>
<th>Series</th>
<th>Interleaved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slice group 1</td>
<td>Gatura</td>
<td>Standard</td>
</tr>
<tr>
<td>Slices</td>
<td>Special</td>
<td>sat.</td>
</tr>
<tr>
<td>Dist. factor</td>
<td></td>
<td>None</td>
</tr>
<tr>
<td>Position</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orientation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase enc. dir.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rotation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Slice group 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Slices</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dist. factor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Position</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orientation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase enc. dir.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rotation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Slice group 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Slices</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dist. factor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Position</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orientation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase enc. dir.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rotation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contrast</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MTC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Magn. preparation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flip angle</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fat suppr.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Water supp.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Averaging mode</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reconstruction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Measurements</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resolution</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Base resolution</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase resolution</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase partial Fourier</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Filter 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raw filter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Filter 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Large FOV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Filter 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normalize</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Filter 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elliptical filter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Filter 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Image Filter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trajectory</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interpolation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PAT mode</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Geometry</td>
<td>Multi-slice mode</td>
<td>Sequential</td>
</tr>
</tbody>
</table>
### SIEMENS MAGNETOM Symphony syngo MR A35

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bandwidth</td>
<td>180 [Hz/Px]</td>
</tr>
<tr>
<td>Flow comp.</td>
<td>No</td>
</tr>
<tr>
<td>RF pulse type</td>
<td>Fast</td>
</tr>
<tr>
<td>Gradient mode</td>
<td>Fast</td>
</tr>
<tr>
<td>Excitation</td>
<td>Slice-sel.</td>
</tr>
<tr>
<td>RF spoiling</td>
<td>1</td>
</tr>
</tbody>
</table>
A volumetric and dosimetric evaluation of target volume delineations and radiation treatment plans in gynecological oncology

SIEMENS MAGNETOM Symphony syngo MR A35

\\USER\ABDOMEN\RADIOThERAPY\cervix - uterus\T2W TSE sag

<table>
<thead>
<tr>
<th>Scan Time: 1:57</th>
<th>Voxel size: 1.4x1.4x4.0 [mm]</th>
<th>Rel. SNR: 1.00</th>
<th>SIEMENS: tse</th>
</tr>
</thead>
</table>

**Routine**

<table>
<thead>
<tr>
<th>Slice group 1</th>
<th>Slices</th>
<th>Dist. factor</th>
<th>Position</th>
<th>Orientation</th>
<th>Phase enc. dir</th>
<th>Rotation</th>
<th>Phase oversampling</th>
<th>FoV read</th>
<th>FoV phase</th>
<th>Slice thickness</th>
<th>TR</th>
<th>TE</th>
<th>Averages</th>
<th>Concatenations</th>
<th>Filter</th>
<th>Coil elements</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>30</td>
<td>25 [%]</td>
<td>Isocenter</td>
<td>Sagittal</td>
<td>A &gt;&gt; P</td>
<td>0 [deg]</td>
<td>0 [%]</td>
<td>350 [mm]</td>
<td>60.0 [mm]</td>
<td>4 [mm]</td>
<td>14</td>
<td>60</td>
<td>1</td>
<td>2</td>
<td>Elliptical filter</td>
<td>BO1,BO2,SP4,SP5</td>
</tr>
</tbody>
</table>

**Contrast**

<table>
<thead>
<tr>
<th>TD</th>
<th>MTC</th>
<th>Mag. preparation</th>
<th>Flip angle</th>
<th>Fat suppr.</th>
<th>Fat sat. mode</th>
<th>Water suppr.</th>
<th>Averaging mode</th>
<th>Reconstruction</th>
<th>Measurements</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>None</td>
<td>150 [deg]</td>
<td>None</td>
<td>Strong</td>
<td>None</td>
<td>Long term</td>
<td>Magnitude</td>
<td>1</td>
</tr>
</tbody>
</table>

**Resolution**

<table>
<thead>
<tr>
<th>Base resolution</th>
<th>Phase resolution</th>
<th>Phase partial Fourier</th>
<th>Filter 1</th>
<th>Filter 2</th>
<th>Filter 3</th>
<th>Filter 4</th>
<th>Filter 5</th>
<th>Image Filter</th>
<th>Trajectory</th>
<th>Interpolation</th>
<th>PAT mode</th>
<th>Geometry</th>
</tr>
</thead>
<tbody>
<tr>
<td>256</td>
<td>98 [%]</td>
<td>Off</td>
<td>Off</td>
<td>Off</td>
<td>Off</td>
<td>On</td>
<td>Off</td>
<td>Off</td>
<td>Cartesian</td>
<td>1</td>
<td>None</td>
<td>Interleaved</td>
</tr>
</tbody>
</table>

**System**

<table>
<thead>
<tr>
<th>Save uncoupled</th>
<th>Scan at current TP</th>
<th>MSMA</th>
<th>Sagittal</th>
<th>Coronal</th>
<th>Transversal</th>
<th>H &gt;&gt; F</th>
<th>CP Spine Array / SP3</th>
<th>CP Spine Array / SP4</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>S - C - T</td>
<td>L &gt;&gt; R</td>
<td>A &gt;&gt; P</td>
<td>Transversal</td>
<td></td>
<td>CP Spine Array / SP4</td>
<td>CP Spine Array / SP4</td>
</tr>
</tbody>
</table>

Page | 31
A volumetric and dosimetric evaluation of target volume delineations and radiation treatment plans in gynecological oncology

SIEMENS MAGNETOM Symphony syngo MR A35

\texttt{\textbackslash UNSER\textbackslash ABDOMEN\textbackslash RADIOThERAPY\textbackslash cervix - uterus\textbackslash T2W TSE tra}

\begin{tabular}{|l|c|}
\hline
Routine & \texttt{CP Spine Array / SP5} 1 \\
\hline
Slice group 1 & \texttt{CP Spine Array / SP6} 0 \\
Slices & \texttt{CP Spine Array / SP7} 0 \\
Dist. factor & \texttt{CP Spine Array / SP1} 0 \\
Position & \texttt{CP Spine Array / SP2} 0 \\
Orientation & \texttt{CP Body Array / B02} 1 \\
Phase enc. dir. & \texttt{CP Body Array / B01} 1 \\
Rotation & Body 0 \\
Phase oversampling & Shim mode Tune up \\
FoV read & Adjust with body coil 0 \\
FoV phase & Confirm freq. adjustment 0 \\
Slice thickness & Assume Silicone 0 \\
TR & Ref. amplitude [1H] 175.355 [V] \\
TE & \texttt{Adjust volume} \\
Averages & \texttt{Position} Isocenter \\
Concatenations & \texttt{Orientation} Transversal \\
Filter & \texttt{Rotation} 0 [deg] \\
Elipical filter & \texttt{R >> L} 350 [mm] \\
Coil elements & \texttt{A >> P} 253 [mm] \\
B01,B02,SP4,SP5 & \texttt{F >> H} 350 [mm] \\
\hline
Contrast & \texttt{Physio} \\
TD & \texttt{1st Signal/Mode} None \\
MTC & \texttt{Dark blood} 0 \\
Magn. preparation & \texttt{Resp. control} Off \\
Flip angle & \texttt{Inline} \\
Fat supp. & Subtract 0 \\
Fat sat. mode & Std-Div-Sag 0 \\
Strong & Std-Div-Cor 0 \\
Water supp. & Std-Div-Tra 0 \\
None & Std-Div-Time 0 \\
Averaging mode & MIP-Sag 0 \\
Magnitude & MIP-Cor 0 \\
Long term & MIP-Tra 0 \\
Measurements & MIP-Time 0 \\
1 & Save original images 1 \\
\hline
Resolution & \texttt{Sequence} \\
Base resolution & \texttt{Introduction} 1 \\
256 & Dimension 2D \\
Phase resolution & Compensate T2 decay 0 \\
0 [\%] & Contrasts 1 \\
Phase partial Fourier & Bandwidth 130 [Hz/Px] \\
Off & Flow comp. No \\
Filter 1 & Allowed delay 20 [s] \\
Raw filter & Echo spacing 14 [ms] \\
Off & \texttt{Sequence} \\
Filter 2 & Turbo factor 15 \\
Large FoV & RF pulse type Low SAR \\
Off & Gradient mode Normal \\
Filter 3 & \texttt{System} \\
Normalize & Save uncombined 0 \\
Off & Scan at current TP 1 \\
Filter 4 & MSMA S - G - T \\
Elliptical filter & Sagittal L >> R \\
On & Coronal A >> P \\
Filter 5 & Transversal H >> F \\
Image Filter & CP Spine Array / SP3 0 \\
Off & CP Spine Array / SP4 1 \\
Trajectory & \texttt{Geometry} \\
Cartesian & Interleaved Multi-slice mode \\
\texttt{Interleaved} & Series Interleaved \\
\texttt{None} & Special sat. None \\
\hline
\end{tabular}
7.3 Medisch protocol RCWEST gynaecologie

**Radiotherapie bij het cervixcarcinoom**

**Documentinformatie**

Documentnummer:
Beheer:
Plaats in DKS:

**Inleiding**

De incidentie van het cervixcarcinoom in Nederland bedraagt 9 per 100.000 vrouwen per jaar. De leeftijdsverdeling van het carcinoom van de cervix vertoont een curve verlopend van 15-90 jaar met een piek rond de 40-45 jaar. De belangrijkste risicofactor voor het cervixcarcinoom is een infectie met een oncoze HPV type en roken. In 85% van de gevallen is cervixcarcinoom een plaveiselcellenarcinoom, in 13% een adenocarcinoom, in 1,5% een adenosquameus carcinoom en in 0,5% een van de andere carcinomen. Het cervixcarcinoom breidt zich voornamelijk uit via directe doorgroei in de omgeving en via bloed- en lymfeklieren. Van de patiënten met een laag stadium heeft 15-20% uitzaalgingen in de pelvis en lymfeklieren. De para-aortale klieren zijn secundaire stations en zijn zelden aangedaan zonder aanwezigheid van uitzaalgingen in de pelvis. Prognostische factoren zijn: FIGO-stadium, lymfkliermetastasen, vaso-invasie en tumorvolume.

**Behandeling**

De behandeling van het cervixcarcinoom bestaat primair uit chirurgie of radiotherapie. Bij tumoren beperkt tot de cervix of met minimale uitbreiding naar de proximale vagina wordt primair gekozen voor radicale chirurgie. Bij uitbreiding buiten de cervix wordt primair gekozen voor radiotherapie, op indicatie in combinatie met chemotherapie of hyperthermie.

**Stadium Ia-1 (diagnose na goedte beoordelen conus)**
Conisatie (bij kinderwens of andere individuele reden)
Uterusextirpatie (indien geen kinderwens)
In geval van lymfangio invasieve groei wordt een pelviene lymfadenectomie geadviseerd.

**Stadium Ia-2 (diagnose na optimale c.q. goed te beoordelen conus)**
Conisatie (bij kinderwens of andere individuele reden)
Uterusextirpatie (indien geen kinderwens)
In geval van lymfangio invasieve groei wordt een pelviene lymfadenectomie geadviseerd.
Er bestaat in Nederland geen consensus over de radicaliteit van de uit te voeren hysterecomie in geval van lymfangio invasieve groei bij het stadium Ia-2.

**Stadium Ib-1 en Ila-1**
Radicale uterusextirpatie met pelviene lymfadenectomie of primaire radiotherapie. De keuze wordt gemaakt op basis van co-morbiditeit of leeftijd. Bij patiënten zonder contra-indicatie voor een operatie wordt gekozen voor primaire chirurgie met het oog op het effect van radiotherapie op de ovaria en/of de sexuele functie. In geval van kinderwens bij tumoren < 2 cm kan worden gekozen...
Radiotherapie bij het cervixcarcinoom

voor een trachelectomie.

Stadium I b - 2, IIa 2 - IVa

Chemoradiatie

Bij een exofytische tumor kan een keuze gemaakt worden voor primaire chirurgie.

Chemotherapie. Het meest gebruikte schema bestaat uit 5-6 kuren single agent cisplatinum 40 mg/m² (in 250 ml 3% NaCl in 90-180 minuten i.v.) eens per week tijdens de radiotherapie

Hyperthermie: Hyperthermie is een alternatief voor chemotherapie bij stadium IIIB tumoren en kan in overige gevallen overvogen worden indien er een contra-indicatie bestaat voor chemotherapie. Tijdens uitwendige bestraling 1x/week diepe hyperthermie. Totaal 5 sessies.

Stadium IVb

Individualisatie van palliatieve behandeling

Postoperatieve radiotherapie is geïndiceerd in geval van:
- Positieve klieren
- Doorgroei van tumor in de parametria
- Doorgroei in (tot aan) de chirurgische snijranden

Op grond van een GOG-studie (ref. Monk) kan in aanwezigheid van prognostisch ongunstige factoren (ten minste twee van de drie factoren vaso-invasie, tumordiameter > 4 cm, invasiediepte > 2/3 of > 15 mm) postoperatieve radiotherapie op het oorspronkelijk tumorgebied en de parametria worden overvogen. Hiermee wordt een betere bekkencontrole bereikt. Indien de indicatie voor postoperatieve radiotherapie lymfkliermetastasen betreft kan worden gekozen voor een combinatie met chemotherapie.

Indicatiestelling

Zie behandeling

Stadiëring

Zie bijlage voor TNM + FIGO-stadiering

Voorbereidende diagnostiek

Lichamelijk onderzoek

Het gynaecologisch onderzoek bestaat uit inspectie en palpatie van de genitalia interna en de parametria. Tenzij de patiënt goed poliklinisch te onderzoeken is, wordt dit onderzoek onder narcose
Verricht door een oncologisch gynaecoloog en radiotherapeut tezamen. Hierbij wordt een schatting gemaakt van de grootte van de tumor en beoordeeld of er ingroei is in de parametria en de vagina. Indien er verdenking bestaat op doorgroei van de tumor in de blaas of in het rectum wordt tevens een cystoscopie resp. proctoscopie uitgevoerd. Bij het algemene lichamelijk onderzoek wordt gelet op vergrote klieren in de liezen en in de fossa supradiviculairs met name links.

Labotoriumonderzoek
Routine (pre-operatief) bloed- en urineonderzoek. In geval van chemotherapie: nierfunctie.

Beeldvormend onderzoek
MRI is het onderzoek van 1e keuze voor vaststellen van de lokale en regionale tumouruitbreiding. (PET-) CT is onderzoek van 1e keuze voor vaststellen van regionale en afstandsmetastasen.

Pathologie
Van de patholoog wordt informatie gevraagd over histo- logosch type en lymfango-invasie. Ingeval van chirurgie daarnaast tumordiameter, infiltratiediepte, aantal en lokalisatie verwijderde- resp. aangedane lymfeklieren metastasen, parametria en snijranden.

Voorbereiding
Er wordt een spiraaltje ingebracht bij elke nieuwe patiënt. Dit wordt gedaan door de gynaecoloog van het verwijzend ziekenhuis. Alle patiënten krijgen een drinkinstructie mee (uitplassen en twee bekertjes water drinken). Bij de PV vraagt de PV laborant voórdat de patiënt het gesprek in gaat om de blaa te legden, en vervolgens krijgt de patiënt twee bekertjes water. Op deze manier kan de patiënt met een gevuilde blaa de CT-sim op. Alle patiënten liggen in rugligging. Er wordt bij elke patiënt ook een MRI gemaakt, op dezelfde dag als de CT-sim. Fusie vindt plaats op het spiraaltje, waarbij de onzekerheid van de match in het achterhoofd gehouden moet worden. Deze methode is niet gevalideerd. Intekening van CTV cervix/uterus vindt plaats op de gefuseerde beelden en de intekening van de CTV klieren vindt plaats op de CT.

Planning

Doelgebied
Cervix, uterus, parametria, proximaal ½ vagina, obturator regio, lymfkliegerbieden langs proximale deel iliaca externa (tot niveau waar keten sterk naar ventraal afbuigt), langs gehele iliaca interna en langs iliaca communis tot niveau promontorium. Bij verdenking op lymfkliegermetastasen op de CT-scan wordt de boven-grens bepaald door het hoogst aangedane lymfkliegergebied met ruime marge. Bij doorgroei in de vagina (mucosaal/submucosaal): doelvolume omvat 2/3 vagina (ondergrens bestralingsveld blijft proximaal van de introitus); bij doorgroei tot ½ of meer van de vagina: gehele vagina tot en met introitus in veld. Bij doorgroei tot in distale 1/3...
Radiotherapie bij het cervixcarcinoom

van de vagina: doelvolume omvat iliaca externa tot en met inguinale regio (oppervlakkige en diepe klieren).

Marges:

GTV-CTV: 1 cm

CTV – PTV marge cervix/uterus:
  1.0 cm in de links-rechts richting
  1.5 cm in de craniao-caudale richting
  2.0 cm in de vertro-dorsale richting

CTV – PTV marge klieren:
  0.5 cm in alle richtingen

Kritieke organen inclusief constraints

Blaas: EQD2 90 Gy
Dunne darm, sigmoid en rectum: EQD2 75 Gy

Techniek

Uitwendig: IMRT

Brachytherapie: HDR met behulp van Utrecht-applicator of verlengde cilinder (bij vaginale uitbreiding > proximale helft vagina).

Dosis specificatie: Conform ICRU en GEC-ESTRO richtlijnen (D2%)

Primaire radiotherapie: 46 Gy in 23 fracties, 5 fracties per week. Bij veel dunne darmbelasting 48,6 Gy in 27 fracties. Brachytherapie, drie maal 7 Gy, 1x per week, niet eerder dan na 30 Gy uitwendige radiotherapie.

Uitvoering

Planning combinatie behandeling (hyperlink)
Positieverificatie (hyperlink)
**Radiotherapie bij het cervixcarcinoom**

### Bijwerkingen

**Acuut:**
- Diarree, waarvoor zo nodig Loperamide
- Dysurie, voldoende drinken belangrijk
- Mucositis vaginaslijmvlies, waarvoor tampons met vaseline

**Laat:**
- Wegvallen ovariële functie bij premenopauzale vrouwen, bij jonge vrouwen hormonale substitutie overwegen iom gynaecoloog
- Diarree
- Problemen met seksualiteit

### Follow-up

Patienten worden gezamenlijk of alternrend ter controle gezien door de gynaecoloog en de radiotherapeut volgens onderstaand schema, in principe minimaal 5 jaar.
- 1e en 2e jaar: eens per 3 maanden
- 3e en 4e jaar: eens per half jaar
- Hierna jaarlijks

### Varia

### Toekomst

### Referenties


### TNM + FIGO

<table>
<thead>
<tr>
<th>TNM</th>
<th>Stadium</th>
<th>FIGO (versie 2009)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td>Geen stadlering mogelijk</td>
<td></td>
</tr>
<tr>
<td>T0</td>
<td>Geen primaire tumor</td>
<td></td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ</td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>Tumor beperkt tot de cervix (uitbreiding naar endometrium blijft T1)</td>
<td></td>
</tr>
<tr>
<td>T1a1</td>
<td>1A1</td>
<td>Invasiediepte &lt; 3mm, lineaire extensie &lt; 7mm</td>
</tr>
<tr>
<td>T1a2</td>
<td>1A2</td>
<td>Invasiediepte 3-5mm, lineaire extensie &lt; 7mm</td>
</tr>
<tr>
<td>T1b1</td>
<td>1B1</td>
<td>Tumor beperkt tot de cervix maar groter dan T1a1, &lt; 4 cm</td>
</tr>
<tr>
<td>T1b2</td>
<td>1B2</td>
<td>Tumor beperkt tot de cervix maar groter dan T1a1, &gt; 4 cm</td>
</tr>
<tr>
<td>T2</td>
<td>II</td>
<td>Tumor breidt zich uit buiten de uterus maar reikt niet tot de bekkenwand of het onderste derde deel van de vagina</td>
</tr>
<tr>
<td>T2a</td>
<td>IIIA1</td>
<td>Tumor infiltreert parametria niet, &lt; 4 cm</td>
</tr>
<tr>
<td></td>
<td>IIIA2</td>
<td>Tumor infiltreert parametria, &gt; 4 cm</td>
</tr>
<tr>
<td>T2b</td>
<td>IIIB</td>
<td>Tumor infiltreert parametria</td>
</tr>
<tr>
<td>T3</td>
<td>III</td>
<td>Tumor reikt tot bekkenwand en/of onderste derde deel vagina en/of veroorzaakt hydronephrose of een niet functionerende nier</td>
</tr>
<tr>
<td>T3a</td>
<td>IIIA</td>
<td>Tumor reikt tot in onderste derde deel vagina maar niet tot de bekkenwand</td>
</tr>
<tr>
<td>T3b</td>
<td>IIIB</td>
<td>Reikt tot de bekkenwand, en/of veroorzaakt hydronephrose of een niet functionerende nier</td>
</tr>
<tr>
<td>T4</td>
<td>IV</td>
<td>Tumor reikt tot in de mucosa van de blaas of het rectum en/of groeit buiten het kleine bekken</td>
</tr>
</tbody>
</table>
7.4 IMRT planningsprotocol RCWEST

HagaZiekenhuis

Planning cervix/endometrium/vulvacarcinoom

Documentinformatie

Documentnummer: Beheer: Tumorfocussteam bekken Plaats in DKS:

Toepasbaarheid

Dit positieverificatieprotocol is toepasbaar op de volgende tumorsites of tumorgroepen zoals die worden genoemd in het kwaliteitssysteem:
- Cervix
- Endometrium
- Vulva

Dit protocol is niet toepasbaar op:
- Ovariumcarcinoom
- Vaginacarcinoom

Medisch behandelprotocol

1. Cervix - RCWEST
2. Endometrium - RCWEST
3. Vulva – RCWEST

Planningstechniek

IMRT

Planning variabelen: Cervix / Endometrium / Vulva

1. Set-up: Indien patiënt uit MCH komt kies CT scanner MCHACOsim.
2. Plaats de lasers op midden loodje en ter hoogte van de tafel.
3. Maak ROI omtrek aan en teken deze eerst in!
4. Klik Gyn 3>> Expansion helpstructures aan
5. Klik script prostaat >> SIB prostaat >> Prost 3>> Bundels aan
6. Kies vervolgens de juiste prescriptie in het scriptmenu en kies:
   - Gyn 4a> Schema 27x1.8Gy of
   - Gyn 4b> Schema 28x1.8Gy of
   - Gyn 4c> Schema 23x2Gy
Planning cervix/endometrium/vulvacarcinoom

7. Kies afhankelijk van de indicatie, endometriuma of cervixca, de volgende bundelpopzet:
   - Gyn 5/5 >> Bundels (on-line EPI's) >> endometriuma
   - Gyn 50 >> Bundels (off-line EPI's) >> cervixcarcinoom
   -

8. Klik Gyn 5/5 >> IMRT settings aan
   - Maximaal aantal segmenten: 35
   - Minimale segmentgrootte: 25 cm²
   - Rest standaard

9. Doserings op maan ROI: PTV(ruim)

Planning Cervix/Endometrium/Vulva: ‘Tips and tricks’

1. Indien de gewenste ‘coverage’ niet gehaald wordt, dan de volgende stappen nemen:
   - Doseren op PTV_riem
   - PTV_ring hogere dosis geven

2. Indien de coverage tekort komt aan de blaas en/of rectumzijde:
   - Gewicht objective (Max 40Gy) Rectum-PTV0.5 EUD verlagen indien mogelijk.
   - Gewicht objective (Max 27.5 Gy) Blaas-PTV0.5 EUD verlagen indien mogelijk.
Planning cervix/endometrium/vulvarcarcinoom

Via Utilities >> Gyn >> volgende scripts afwerken:

- Gyn 1 >> Contours
- Gyn 2a >> CERVIX Expansion to PTV
- Gyn 2b >> ENDMET Expansion to PTV
- Gyn 3 >> Expansion help structures
- Gyn 4a >> Schema 27x1.8Gy
- Gyn 4b >> Schema 28x1.6Gy
- Gyn 4c >> Schema 23x2Gy
- Gyn 5a >> Bundels (on-line EPI's)
- Gyn 5b >> Bundels (off-line EPI's)
- Gyn 6 >> IMRT settings
- Gyn 7 >> Doseplanes
7.5 Working out sheets SPSS

a) Kolmogorov–Smirnov test for lymph nodes by physician and modality

<table>
<thead>
<tr>
<th></th>
<th>CTV Ph 1</th>
<th>CTV Ph 2</th>
<th>CTV Ph 3</th>
<th>CT Ph 1</th>
<th>CT Ph 2</th>
<th>CT Ph 3</th>
<th>MRI Ph 1</th>
<th>MRI Ph 2</th>
<th>MRI Ph 3</th>
<th>PET Ph 1</th>
<th>PET Ph 2</th>
<th>PET Ph 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>8</td>
<td>8</td>
<td>6</td>
<td>8</td>
<td>8</td>
<td>6</td>
<td>6</td>
<td>8</td>
<td>8</td>
<td>6</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>Normal Mean</td>
<td>378.7</td>
<td>253.1</td>
<td>370.1</td>
<td>157.63</td>
<td>89.50</td>
<td>351.00</td>
<td>378.75</td>
<td>253.13</td>
<td>405.50</td>
<td>60.826</td>
<td>288.40</td>
<td></td>
</tr>
<tr>
<td>Parametersa'b</td>
<td>5</td>
<td>3</td>
<td>7</td>
<td>60.82</td>
<td>287.4</td>
<td>91.486</td>
<td>297.41</td>
<td>169.68</td>
<td>60.826</td>
<td>288.40</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Std.</td>
<td>169.6</td>
<td>60.82</td>
<td>7</td>
<td>94</td>
<td>2</td>
<td>2</td>
<td>19</td>
<td>3</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Most Extreme Absolute</td>
<td>.317</td>
<td>.212</td>
<td>.208</td>
<td>.191</td>
<td>.234</td>
<td>.257</td>
<td>.317</td>
<td>.212</td>
<td>.180</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>.317</td>
<td>.212</td>
<td>.208</td>
<td>.135</td>
<td>.234</td>
<td>.257</td>
<td>.317</td>
<td>.212</td>
<td>.173</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>-.220</td>
<td>-.171</td>
<td>-.123</td>
<td>-.191</td>
<td>-.156</td>
<td>-.132</td>
<td>-.220</td>
<td>-.171</td>
<td>-.180</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Differences</td>
<td>Kolmogorov-Smirnov Z</td>
<td>.597</td>
<td>.598</td>
<td>.510</td>
<td>.540</td>
<td>.661</td>
<td>.630</td>
<td>.897</td>
<td>.598</td>
<td>.440</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asymp. Sig. (2-tailed)</td>
<td>.396</td>
<td>.867</td>
<td>.957</td>
<td>.933</td>
<td>.775</td>
<td>.822</td>
<td>.396</td>
<td>.867</td>
<td>.990</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a. Test distribution is Normal.
b. Calculated from data.

b) Kolmogorov–Smirnov test for primary tumor by physician and modality

<table>
<thead>
<tr>
<th></th>
<th>CT Ph 1</th>
<th>CT Ph 3</th>
<th>CT Ph 2</th>
<th>MRI Ph 1</th>
<th>MRI Ph 3</th>
<th>MRI Ph 2</th>
<th>PET Ph 1</th>
<th>PET Ph 2</th>
<th>PET Ph 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>8</td>
<td>6</td>
<td>8</td>
<td>7</td>
<td>5</td>
<td>7</td>
<td>8</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Normal Mean</td>
<td>240.2</td>
<td>243.3</td>
<td>240.1</td>
<td>183.2</td>
<td>303.4</td>
<td>195.1</td>
<td>113.1</td>
<td>244.0</td>
<td>132.3</td>
</tr>
<tr>
<td>Parametersa'b</td>
<td>5</td>
<td>3</td>
<td>3</td>
<td>9</td>
<td>0</td>
<td>4</td>
<td>3</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>Std. Deviation</td>
<td>177.2</td>
<td>102.7</td>
<td>128.2</td>
<td>97.17</td>
<td>109.3</td>
<td>98.75</td>
<td>58.72</td>
<td>101.2</td>
<td>65.59</td>
</tr>
<tr>
<td>Most Extreme Absolute</td>
<td>.369</td>
<td>.268</td>
<td>.257</td>
<td>.201</td>
<td>.215</td>
<td>.274</td>
<td>.182</td>
<td>.261</td>
<td>.332</td>
</tr>
<tr>
<td>Positive</td>
<td>.369</td>
<td>.268</td>
<td>.257</td>
<td>.154</td>
<td>.215</td>
<td>.274</td>
<td>.166</td>
<td>.261</td>
<td>.234</td>
</tr>
<tr>
<td>Negative</td>
<td>-.249</td>
<td>-.226</td>
<td>-.187</td>
<td>-.201</td>
<td>-.137</td>
<td>-.192</td>
<td>-.182</td>
<td>-.220</td>
<td>-.332</td>
</tr>
<tr>
<td>Differences</td>
<td>Kolmogorov-Smirnov Z</td>
<td>1.043</td>
<td>.657</td>
<td>.726</td>
<td>.531</td>
<td>.480</td>
<td>.724</td>
<td>.516</td>
<td>.640</td>
</tr>
<tr>
<td>Asymp. Sig. (2-tailed)</td>
<td>.227</td>
<td>.781</td>
<td>.667</td>
<td>.940</td>
<td>.875</td>
<td>.672</td>
<td>.953</td>
<td>.807</td>
<td>.340</td>
</tr>
</tbody>
</table>

a. Test distribution is Normal.
b. Calculated from data.
c) Test results paired t-test

**Primair**

<table>
<thead>
<tr>
<th>Paired Samples Correlations</th>
<th>N</th>
<th>Correlation</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pair 1 Mean CT &amp; Mean MRI</td>
<td>7</td>
<td>.661</td>
<td>.106</td>
</tr>
<tr>
<td>Pair 2 Mean CT &amp; Mean PET</td>
<td>8</td>
<td>.706</td>
<td>.050</td>
</tr>
<tr>
<td>Pair 3 Mean MRI &amp; Mean PET</td>
<td>7</td>
<td>.824</td>
<td>.023</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Paired Samples Test</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Paired Differences</strong></td>
</tr>
<tr>
<td>---------------------</td>
</tr>
<tr>
<td>Pair 1 Mean CT - Mean MRI</td>
</tr>
<tr>
<td>Pair 2 Mean CT - Mean PET</td>
</tr>
<tr>
<td>Pair 3 Mean MRI - Mean PET</td>
</tr>
</tbody>
</table>

**Klieren**

<table>
<thead>
<tr>
<th>Paired Samples Correlations</th>
<th>N</th>
<th>Correlation</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pair 1 Mean CT &amp; Mean MRI</td>
<td>7</td>
<td>.533</td>
<td>.218</td>
</tr>
<tr>
<td>Pair 2 Mean CT &amp; Mean PET</td>
<td>8</td>
<td>.986</td>
<td>.000</td>
</tr>
<tr>
<td>Pair 3 Mean MRI &amp; Mean PET</td>
<td>7</td>
<td>.503</td>
<td>.250</td>
</tr>
</tbody>
</table>
### Paired Samples Test

<table>
<thead>
<tr>
<th>Pair</th>
<th>Paired Differences</th>
<th>Std. Deviation</th>
<th>Std. Error Mean</th>
<th>95% Confidence Interval of the Difference</th>
<th>t</th>
<th>df</th>
<th>Sig. (2-tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Mean CT - Mean MRI</td>
<td>112,762</td>
<td>115,012</td>
<td>43,471</td>
<td>6</td>
<td>219,131</td>
<td>2,594</td>
</tr>
<tr>
<td>2</td>
<td>Mean CT - Mean PET</td>
<td>-8,833</td>
<td>23,583</td>
<td>8,338</td>
<td>-</td>
<td>10,883</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>Mean MRI - Mean PET</td>
<td>-122,286</td>
<td>126,593</td>
<td>47,847</td>
<td>-</td>
<td>-239,364</td>
<td>2,556</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>