MR based electric properties imaging for hyperthermia treatment planning and MR safety purposes
Balidemaj, E.

Citation for published version (APA):

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: http://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.
3 Feasibility of Electric Property Tomography of Pelvic Tumors at 3T

This chapter is published as:
Chapter 3

Abstract

**Purpose:** Investigation of the validity of the “transceive phase assumption” for Electric Property Tomography of pelvic tumors at 3T. The acquired electric conductivities of pelvic tumors are beneficial for improved SAR determination in Hyperthermia Treatment Planning.

**Methods:** Electromagnetic simulations and MRI measurements of a pelvic-sized phantoms and the human pelvis of a volunteer and a cervix cancer patient.

**Results:** The reconstructed conductivity values of the phantom tumor model are in good quantitative agreement (mean deviation: 1-10%) with the probe measurements. Furthermore, the average reconstructed conductivity of a pelvic tumor model was in close agreement with the input conductivity (0.86 S/m vs. 0.90 S/m). The reconstructed tumor conductivity of the presented patient (cervical carcinoma, Stage: IVA) was 1.16 ± 0.40 S/m.

**Conclusion:** This study demonstrates the feasibility of EPT to measure quantitatively the conductivity of centrally located tumors in a pelvis-sized phantom and human pelvis with a standard MR system and MR sequences. A good quantitative agreement was found between the reconstructed \( \sigma \)-values and probe measurements for a wide range of \( \sigma \)-values and for off-axis located spherical compartment. As most pelvic tumors are located in the central region of the pelvis these results can be exploited in Hyperthermia Treatment Planning systems.

3.1 Introduction

Radiofrequency (RF) deep hyperthermia is a thermotherapy where pelvic tumors (e.g. cervical, bladder and prostate tumors) are heated by RF phased antenna arrays operating in the 70 to 150 MHz frequency range (1,2). To generate spatially focussed heating in the tumor, quantified by the Specific Absorption Rate (SAR), electromagnetic (EM) modelling is employed prior to treatment. This procedure is called Hyperthermia Treatment Planning (HTP). An essential step in HTP is the assignment of tumor electrical conductivity, as this is the main determining factor in the SAR deposition in the tumor. Currently, a fixed tumor conductivity (e.g. muscle conductivity of 0.72 [S/m] at 128MHz) is assumed for all patients and tumor sites. However, as tumors have elevated conductivities varying significantly among patients (3), this assumption leads to an unreliable SAR determination. This was illustrated in previous studies (2,4) which showed that the use of nonpatient-specific electric properties can lead to 2°C lower tumor temperatures during hyperthermia. Therefore, patient specific characterization of the tumor conductivity is desirable to improve Hyperthermia Treatment.

Retrieving information of the electric properties of tumors for characterization and diagnostics purposes, has received great attention the last decade (3,5,6). A large difference between the conductivity of healthy and malignant tissues has been shown for breast (7–9), liver (10,11), bladder tumors (12) and gliomas (13). A non-invasive technique to retrieve the tissue electric properties from MR data was proposed by
Feasibility of EPT of pelvic tumors

Haacke et al. (14) already in 1991. In 2003, Wen (15) presented electric property reconstruction with phantom and animal experiments at 1.5T and 4.7T. More recently, Katscher et al. built up these initial ideas and introduced Electric Property Tomography (EPT) (16,17) to extract EPs from the measured transmit $B_1^+$ amplitude and phase maps. The feasibility of EPT to detect and characterize tumors has been investigated for breast tumors (3,18,19) and gliomas (5,6). These studies confirmed the elevated tumor conductivity in vivo. Furthermore, in (20,21) the feasibility of EPT to reconstruct the conductivity of liver was investigated.

In this study we investigate the feasibility of using EPT to measure the tumor conductivity of hyperthermia patients to be able to use patient specific tumor conductivities in the hyperthermia treatment planning. Since there is an overlap in the frequency range between MRI and hyperthermia, the values found by MR EPT should be representative for the conductivity at the hyperthermia frequency. Here we employ a 3T MR scanner to perform EPT retrieving conductivity values at 128 MHz. An important aspect will be the evaluation of the impact of the so-called “transceive assumption” used in EPT reconstructions at 128 MHz in the human pelvis. This assumption arises as the $B_1^+$ phase is not directly measurable by standard MR sequences. This assumption is widely used in most current implementations of EPT (16,22–25). Furthermore, it was shown that under additional circumstances the conductivity can be reconstructed based only on phase measurements (23,24).

To date, the validity of the transceive phase assumption was shown to hold in human head (16,22–25). However, the phase assumption was shown to be less valid at the periphery of the human head at 7T (24). Due to the larger dimensions of the pelvis the phase error should be reinvestigated for this particular anatomy. As the ratio of the axial dimension of the pelvis and the RF wavelength at 3T are in the same regime as this ratio for the head at 7T MRI, we expect that the validity of the transceive phase assumption in the pelvis at 3T is similar to the validity of the transceive phase assumption in the brain at 7T. In other words, we expect that this assumption is valid in the central region of the pelvis: the location were pelvic tumors are located.

In this work, the applicability of the phase assumption at 3T in the pelvis is investigated using a pelvic-sized phantom and for various dielectric properties occurring in the pelvis anatomy. Furthermore, we present EPT based conductivity measurements for a pelvic tumor model over a wide range of tumor conductivities and tumor locations. Furthermore, quantitative conductivity reconstructions using $B_1^+$ as well as using phase-only information are compared. Additionally, we present in vivo conductivity reconstruction results of the human pelvis of a female volunteer and cervix cancer patient.

3.2 Methods

EM simulations of a pelvic-sized phantom and human pelvis model were performed to study the feasibility of EPT on the pelvis region. Furthermore, the effect of object asymmetry was investigated by displacing an inner compartment to three different locations within the phantom. The electrical conductivity of the inner compartment of
the phantom was varied using different saline concentrations. The complete conductivity range that can occur at 128 MHz (26) in human tissue was covered in this experiment.

MR measurements of the pelvic-sized phantom and female pelvis were conducted to validate the EM simulations. Furthermore, in vivo measurements were used to reconstruct the electrical conductivity and compare it to the literature values.

3.2.1 EPT reconstruction

Assuming that the dielectric properties are piece-wise constant, the tissue electric conductivity can be computed by the homogenous Helmholtz equation (23)

$$\frac{\nabla^2 \mathbf{B}_1^+}{\mathbf{B}_1^+} = -\mu_0 \varepsilon_0 \varepsilon_r \frac{\mu_0}{\varepsilon_0} \omega^2 - i \mu_0 \sigma \omega$$

(1)

where \(\mathbf{B}_1^+\) is the complex transmit field \(\mathbf{B}_1^+ = |\mathbf{B}_1^+| e^{i\phi^+}\), \(\varepsilon_r\) and \(\sigma\) the relative permittivity and the conductivity of the object of interest, respectively, \(\omega\) the Larmor angular frequency, \(\mu_0\) and \(\varepsilon_0\) the permeability and permittivity of vacuum, respectively. The conductivity can be computed by

$$\sigma = -\text{Im} \left( \frac{\nabla^2 \left( |\mathbf{B}_1^+| e^{i\phi^+} \right)}{|\mathbf{B}_1^+| e^{i\phi^+}} \right) \frac{1}{\mu_0 \omega} = \frac{1}{\mu_0 \omega} \left( \nabla^2 \phi^+ + 2 \frac{\nabla |\mathbf{B}_1^+| \cdot \nabla \phi^+}{|\mathbf{B}_1^+|} \right).$$

(2)

were in the last part of Eq.(2), the identity \(\nabla e^{i\phi^+} = e^{i\phi^+} i \nabla \phi^+\) was used (27). In regions where the variation of the \(\mathbf{B}_1^+\) is negligible, thus \(\nabla |\mathbf{B}_1^+| \approx 0\), or when the following condition holds (24)

$$\nabla^2 \phi^+ \gg \frac{2 \nabla |\mathbf{B}_1^+| \nabla \phi^+}{|\mathbf{B}_1^+|}$$

(3)

the conductivity can be computed by using phase-only data as

$$\sigma \approx \frac{1}{\mu_0 \omega} \nabla^2 \phi^+.$$  

(4)

\(\mathbf{B}_1^+\) amplitude can be obtained by various techniques (28–30), however, the \(\mathbf{B}_1^+\) phase \(\phi^+\) is difficult to determine from MR measurements. The measurable phase, also referred to as the “transceive phase” \(\phi^\pm\), of an MR image is a combination of the transmit \(\mathbf{B}_1^+\) phase \(\phi^+\) and its counterpart, the receive \(\mathbf{B}_1^-\) phase \(\phi^-\). The contribution of \(\phi^+\) and \(\phi^-\) is considered equal for quadrature transmission and reverse quadrature detection with a two ports birdcage coil, which is referred to as the transceive assumption (16). In addition to requirements with respect to detection, symmetry in the object under test is also important (23). Asymmetries can lead to unequal contributions of the transmission and reception process in the total transceive phase. The significance of this effect becomes larger at higher field strength. See (23) for more details about
field strength, geometry, dielectric content and validity of the transceive assumption. As in previous studies \((16,23,24,31)\), the transceive phase assumption will be used in this work, thus

\[
\phi^\pm = \phi^+ + \phi^- \\
\phi^+ \approx \frac{\phi^+}{2} \quad \phi^- \approx \frac{\phi^-}{2}.
\]

(5)

The conductivity maps are computed with Eq.\((2)\) for EPT reconstructions based on \(B_1^+\) amplitude and phase data, while Eq.\((4)\) is used for phase-only EPT reconstruction.

### 3.2.2 Phantom

The pelvic-sized phantom used for simulations and measurements consisted of an elliptical cylinder \((d_{\text{major}}=34 \text{ cm}, d_{\text{minor}}=25 \text{ cm}, \text{length}=40 \text{ cm})\), with a spherical \((r=5.0 \text{ cm})\) inner compartment mimicking a pelvic tumor or an arbitrary tissue type (Figure 1a). The interior of the spherical compartment of the phantom was connected to the outer surface using a hollow rod, this allowed for easy change of its content (Figure 1b). The inner compartment could be positioned on- or off-axis to evaluate the effect of asymmetric geometry on the transceive phase assumption and its impact on conductivity reconstruction.

Figure 1. Pelvic-sized phantom used for simulations (a) and experiments (b).

Figure 2. A mid-plane slice of the phantom with the inner compartment positioned centrally (a), down right (b), right (c) and top right (d).

To demonstrate the validity of the phase assumption in a pelvic-sized geometry, the phantom was filled with ethelyne glycol in which 64 gr/l NaCl was dissolved. This lead to dielectric values \((\sigma=0.44 \text{ S/m} \text{ and } \varepsilon_r=30)\) that approach the volumetric average of a female pelvis based on literature values \((26)\) and an anatomical female model \((32)\).

To further validate the feasibility of EPT for the whole range of possible \(\sigma\)–values occurring in biological tissue \((26)\), the conductivity of the content of the spherical compartment was fixed to \(\sigma = 0.01, 0.32, 0.53, 0.67, 1.06, 1.18, 1.34, 1.48, 1.74, 1.81 \text{ S/m}\). The dielectric properties at 128 MHz were independently verified for all 10 saline solutions by acquiring small samples during the MR experiments and measuring them.
with an impedance probe (85070E, Agilent Technologies). The content of the outer compartment remained unchanged for all measurements.

To test the applicability of the transceive phase assumption for asymmetric geometries, the spherical compartment was positioned in three different off-center locations (down right, right and top right) as depicted in Figure 2.

3.2.3 Simulation

Simulations with the pelvic-sized phantom (see previous section) and the human pelvis (Ella, IT’IS Foundation (32)) were performed using in-house developed Finite-Difference Time Domain (FDTD) tools (33). An artificial cervix tumor model was inserted in the female model. The transmit ($B_1^+$) and receive ($B_1^-$) fields were simulated for a realistic 3T MRI body coil model based on 3.0T Achieva (Philips, Best, The Netherlands) consisting of 16 rods low-pass birdcage coil design. The coil was tuned at 128 MHz and was driven in quadrature mode. Further details of the used coil model can be found in (34).

The human pelvis and phantom were placed in the center of the body coil. A resolution of 2.5x2.5x5mm for the human pelvis and phantom was used for simulations. To verify the applicability of the transceive phase assumption, as stated in Eq.(5), the true $B_1^+$ phase ($\phi^+$) and transceive phase ($\phi^\pm$) were compared for the pelvic-sized phantom and the human pelvis.

3.2.4 MR measurements

All experiments were conducted on a 3.0T scanner (Achieva, Philips Healthcare, Best, The Netherlands) using a 16 channel torso receive array. The torso coil set-up consisted of an anterior and posterior coil section. The separate section consisted of two rows of four overlapping coil-elements. The receiver non-uniformity including the phase contribution of the receive array was eliminated by using the so called CLEAR technique (35). The net effect of this technique on the phase is that phase of the receive array is replaced by the receive phase contribution of the birdcage coil operated in reverse quadrature. $B_1^+$ amplitude map was acquired using the actual flip angle imaging (AFI) method (28) (3D, nom. flip angle = 65° TR1 = 50 ms, TR2 = 290 ms, 2.5x2.5x5mm, 12 slices, scan duration = 6 min.). The transceive phase was acquired by a spin echo (SE) sequence (2.5x2.5x5mm, TR = 1200 ms, 12 slices, scan duration = 6 min.) (36,37) using the uniformity correction method [CLEAR] (35). To correct for eddy currents the transceive phase was measured twice with opposing gradients (23). Conductivity values were reconstructed using the Helmholtz based reconstruction based on $B_1^+$ field (Eq. 2) and phase-only measurements (Eq. 4).

First, MR measurements were performed on the pelvic-sized phantom to validate the simulation results. To enhance the MR signal, MnCl$_2$$\bullet$4H$_2$O (95 mg/L) (38) was added to the inner and outer compartment of the phantom for all measurements. The probe measurements as described in previous section were performed on saline solutions containing MnCl$_2$$\bullet$4H$_2$O.
Finally, in vivo MR measurements of a female volunteer and a cervix cancer patient (age: 85, Stage: IVA, Cervical carcinoma) were conducted. Due to scan time limitations, a more coarse resolution of 5mm isotropic was used. Peristaltic motion was reduced with the intravenous injection of Buscopan®. Patient scans for this study were performed in accordance with the approval of the Medical Ethics Board. $B_1^+$ amplitude and phase maps of the pelvis were acquired using the same setup and MR sequences used for the phantom experiments. To further visually assess the quality of the EP maps, anatomical scans were obtained (T1 weighted Ultra fast GRE, TR/TE=4.0/1.96ms, 1x1x2mm, and T2w-TSE, TR/TE=5906/80ms, 0.70x 0.90x3.00 mm). Gross tumor volume (GTV) was delineated by a radiation oncologist based on CT and T2-weighted MRI images.

3.2.5 Postprocessing

To evaluate the effect of the transceive phase approximation, the phase error ($\phi^+-\phi^{±/2}$) maps and the corresponding histograms were determined from the simulated EM fields. Subsequently, to investigate the effect of the phase error on the conductivity reconstruction, EPT reconstructions based on the simulated fields were performed using true phase $\phi^+$ and transceive phase assumption $\phi^{±/2}$ for a pelvic-sized phantom and human pelvis model.

The Laplacian required to evaluate Eq.(2) and Eq.(4) was computed by a kernel-based method as described in (23) using a kernel size of 7x7x5 voxels. This noise-robust kernel was used for convolution of $B_1^+$ data. As the outcome of a second derivative is sensitive to noise it is essential to use noise-robust kernels.

The average $\sigma$-values for all simulations and measurements were computed as the arithmetic mean of all pixels inside a (manually) delineated region. The standard deviation was computed assuming that all data was normally distributed. To exclude the effect of boundary reconstruction errors, the manually delineated regions excluded the boundaries where out-of-range conductivity values might be reconstructed. All computations regarding EPT reconstruction were performed using MATLAB® (The Mathworks, Natick, MA, U.S.).

3.3 Results

3.3.1 Phase error

The $|B_1^+|$ maps of phantom and pelvis are shown in Figure 3a and 3b, respectively. In Figure 3c the phase error ($\phi^+-\phi^{±/2}$), evaluated by simulations for a homogenous phantom, is depicted. This figure shows to what extent the transceive phase assumption holds. As expected, the phase error is larger at the periphery of the phantom, indicating that the transceive phase assumption deteriorates there. Furthermore, it is shown that the phase error exhibits a left/right antisymmetry. Similarly, Figure 3d shows the phase error for the human pelvis. In the human anatomy a larger phase error is observed compared to the phantom. Also for the anatomy, the phase error shows a left/right
antisymmetry; however, the error is not only confined to the periphery. The distribution of the phase error for the phantom and the human pelvis, are shown in Figure 3e and 3f, respectively. The mean±standard deviation of the phase errors are 0.149±2.96° (0.0026±0.0517 rad) (Fig. 3e) and -0.395±3.105° (-0.0069±0.0542 rad) (Fig. 3f).

3.3.2 Phantom simulations and measurements

Figure 4 depicts the results of homogenous phantom simulations (left column) and experiments (right column). The first row shows the reconstruction based on the complex $B_1^+$, thus including the true $\phi^+$. As mentioned, the true $B_1^+$ phase can only be simulated at this stage. In Fig. 4c and 4d the conductivity maps are shown using $B_1^+$ amplitude and transceive phase while Figure 4e and 4f show the phase-only conductivity reconstruction. In Figure 4c is observed that the conductivity slightly deviates from the conductivity reconstruction in Figure 4a implying that the use of $\phi^\pm/2$ instead of $\phi^+$ mildly affects the quality of the conductivity reconstruction.

The $\sigma$-maps based on measurements (Figure 4, right column) show similar results with respect to the $\sigma$-maps based on simulations. When using phase-only information for EPT reconstruction, see Figure 4 (3rd row), the conductivity values deviate stronger at the periphery for simulations as well as measurements. In addition to the local overestimated conductivity values just below and above the centre of the phantom in measurements and simulations, noticeable disagreement is also observed at the utmost left and right part of the phantom. In these peripheral regions the reconstructed values are underestimated by approx. 40%. This overestimation and underestimation pattern is not observed when using both amplitude and phase information in simulations and measurements. However, for the central region of the phantom, conductivity values are shown to correlate well with the actual $\sigma$-values for all reconstruction methods including the phase-only. The error observed in the peripheral regions of the phantom using the phase-only conductivity reconstruction (Fig. 4e,f) are caused by large variations in the $B_1^+$ amplitude which lead to violation of the condition as stated in Eq.(3).

Table 1 summarizes the conductivity values (mean ± standard deviation), confirming an overall good agreement with the actual fluid conductivity at the central region of the body coil. The high conductivity value indicating the boundary of the sphere compartment (Fig. 4, right column), is resulting from the piece-wise media assumption in EPT combined with the numerical implementation of the Laplacian.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Reconstructed conductivity values (mean ± standard deviation) in S/m based on measurements and simulations as presented in Figure 4. Impedance probe measurement: $\sigma = 0.44$ S/m.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measurements</td>
<td>Simulations</td>
</tr>
<tr>
<td>Outer compartment ($</td>
<td>B_1^+</td>
</tr>
<tr>
<td>Inner compartment ($</td>
<td>B_1^+</td>
</tr>
<tr>
<td>Outer compartment ($\phi^\pm/2$)</td>
<td>0.30 ± 0.16</td>
</tr>
<tr>
<td>Inner compartment ($\phi^\pm/2$)</td>
<td>0.42 ± 0.09</td>
</tr>
</tbody>
</table>
Feasibility of EPT of pelvic tumors

Figure 3. The $B_1^+$ amplitude map for the homogenous phantom (a) and human pelvis (b). The phase error map and the corresponding histogram for phantom (c,e) and human pelvis (d,f).

Figure 4. Conductivity reconstruction of the homogeneous phantom. The conductivity was reconstructed based on simulated or measured RF transceive and receive fields. Various combinations of those RF fields were used for the reconstruction, namely, the full complex transmit field ($B_1^+$, simulations only), the amplitude of the transmit field and transceive phase ($\phi^{\pm}/2$) and the transceive phase only.

Figure 5: a) Reconstructed conductivity map of the mid-plane slice of the phantom measurements based on $B_1^+$ amplitude and phase data. b) Conductivity values of the inner compartment verified by probe measurements (white). Reconstructed conductivity values based on both amplitude and phase (grey) and phase-only data (black), Eq.(4).
Figure 5 depicts the reconstructed $\sigma$-maps, based on $B_1^+$ amplitude and phase data, of 10 phantom measurements with increasing $\sigma$-value in the spherical compartment. The probe measurements of saline solutions are shown in white. The reconstructed average $\sigma$-values of the spherical compartment were obtained by manual delineation of the sphere compartment of the mid-plane slice. The average $\sigma$-values using $B_1^+$ field and phase-only data are shown in grey and black, respectively. Based on Figure 5 it can be observed that the reconstructed average $\sigma$-values are in good quantitative agreement with the probe measurements. A deviation between 1% and 10% is observed for the average EPT reconstruction based on $B_1^+$ amplitude and phase compared to the probe measurements. However, the phase-only EPT reconstruction shows a higher deviation, yielding an overestimation of the reconstructed average $\sigma$-value ranging between 1% and 25% compared to probe measurements.

To investigate the effect of asymmetries, the inner sphere compartment was positioned in three different off-axis positions. Figure 6 shows the reconstructed $\sigma$-map, based on $B_1^+$ amplitude and phase data, with the spherical compartment ($\sigma = 0.64 \, \text{S/m, probe measurement}$) positioned on-axis (Fig. 6a) and off-axis (Fig. 6b–d). The histograms of the inner compartment are shown in Figure 6e–h. The histograms of the off-centrally located compartments (Fig. 6f–6h) show no significant disagreement compared to a centrally placed spherical compartment (Fig. 6e). The effect of asymmetry on conductivity reconstruction is marginal (2–7% deviation of mean conductivity) and is not expected to corrupt tumor conductivity reconstruction of tumors located off-centrally.

3.3.3 \textit{In vivo} simulations and measurements

EPT results based on simulations and in vivo experiments with a healthy volunteer and a cervical cancer patient are shown in Figure 7. The first row (a–c) shows the simulated or measured anatomy. For the simulations the underlying electrical conductivity is shown, whereas for the in vivo scans a T1w (b) and T2w (c) scans are shown. Furthermore, the $B_1^+$ amplitude (d–f) and transceiver phase (g–i) are given.

For the simulation, the electrical conductivity was reconstructed based on the complex $B_1^+$ field (j). This reconstruction showed good agreement with the input conductivity (a). Only at conductivity boundaries, large deviations between reconstructed and input conductivity are observed. This deviation is caused by the piece-wise media assumption in the EPT reconstruction and the kernel-based implementation of the reconstruction algorithm. The observed conductivity in the tumor region was in close agreement with the input conductivity of that region (0.86 S/m vs. 0.90 S/m, resp.). As the $B_1^+$ phase cannot be measured, this reconstruction is not shown for the in vivo scans (k,l).

Next, the reconstructed conductivity based on the $B_1^+$ amplitude and the transceiver phase is shown (m–o). By comparing the simulation results (j and m), it can be observed that the conductivity reconstruction is only mildly affected by introducing the transceiver phase assumption. This assumption led to overestimation and underestimation in the
Feasibility of EPT of pelvic tumors

Figure 6. On-axis (a) and off-axis located inner compartment (b-d). (e-h) The histograms of the conductivity values of the inner compartments of a-d, respectively. The red line indicates the conductivity value based on probe measurement. Reconstructions are based on $B_1^+$ amplitude and phase data.

Figure 7. Simulation (left column) and measurement results of a female volunteer (middle column) and cervix patient (right column).
periphery of the anatomy. For example in the left bottom part an overestimation of the conductivity was seen, whereas an underestimation in the right bottom part was observed. This anti symmetric behavior is present in the simulation as well as in the measured data. This result is comparable for the phantom experiments (Fig. 4). The observed conductivity in the centrally placed tumor, however, remained almost unchanged (0.85 S/m). Furthermore, the reconstructed tumor conductivity for slices with an offset in the z-direction of 0.5cm and 1cm (not shown here) were in close agreement with the reconstructed conductivity values of the mid-plane slice (Figure 7, left column), however, an overestimation of 4–12% was observed compared to the reconstructed tumor conductivity values of the mid-plane slice. This measurement also allowed for in vivo determination of the electrical conductivity of the tumor. In this patient (o), an electrical conductivity of 1.16±0.40 S/m was observed for the delineated gross tumor volume as depicted in Figure 8. The latter conductivity value is based on EPT reconstruction using $B_1^+$ amplitude and phase data.

Finally, the reconstructed conductivity based only on the transceive phase is shown (p–r). Omitting the $B_1^+$ amplitude led to a general overestimation of the electrical conductivity. It is observed that the conductivity in the tumor simulation increased to 0.98 S/m.

### 3.4 Discussion

In this study the feasibility of conductivity reconstruction of centrally located pelvic tumors was investigated for use in Hyperthermia Treatment Planning systems. Previous studies have focused on EPT reconstruction of the human brain for local SAR evaluation for RF safety purposes in MRI. Due to the dependency of the transceive phase assumption on measurement setup (e.g. object size, coil setup, RF frequency, etc.), the validity of the transceive phase assumption in the pelvis anatomy was investigated in this study by simulations and MR measurements.

Reconstruction of conductivity maps by EPT requires $B_1^+$ amplitude and phase maps. Since the $B_1^+$ phase ($\phi^+$) cannot be determined directly by MR measurements, an estimation of the $B_1^+$ phase is determined by measuring the transceive phase ($\phi^\pm$). The transceive phase contains contribution of the transmit field ($B_1^+$) and receive field ($B_1^-$). In theory, an equal contribution to the transceive phase is only expected for a cylinder or a sphere in case the $B_1^+$ is linearly polarized or in case of a quadrature reversal between the two ports (23) in a Tx/Rx quadrature birdcage coil (23). For other geometries, the validity of the transceive phase approximation is approximate and depends on various factors such as the frequency of the applied fields. This was extensively investigated for the human brain in (24). Therefore, in this study the
applicability of the transceive phase approximation in EPT at 3T was investigated for the pelvis anatomy and elliptical objects of a similar size.

The phase error \( (\phi^+ - \phi^\pm/2) \) is furthermore affected by the dielectric properties as was shown in (24) for the human head and head-sized phantoms. In this work it was shown in Figure 3 that the phase error in the human pelvis is small in the central region suggesting that EPT of pelvic tumors is possible. To show the feasibility of EPT for conductivity reconstruction of tumors in the pelvic region, a pelvic tumor model was placed in a phantom with pelvic equivalent dielectric properties. To this extent, the conductivity of the inner compartment of the phantom was varied to verify the applicability of the transceive phase assumption for a complete range of conductivity values occurring in biological tissue at 128MHz. Results presented in Figure 5 demonstrate the feasibility of EPT to reconstruct a wide range of tumor conductivity values. The ringing artifacts observed in the outer compartment, Figure 4d,f and Figure 5, are presumably because of fluid motion caused by mechanical vibrations due to gradient switching. These artifacts were not observed in the smaller volume of the inner compartment, nor in the in vivo experiments.

To test the robustness of EPT reconstruction on asymmetric geometries, the inner compartment of the phantom was displaced to three different off-axis locations. This would mimic realistic scenarios in the clinic where the pelvic tumors might be located slightly outside the central region. The results presented in Figure 6 show that the conductivity reconstruction is reliable despite the introduced asymmetry. The quantitative impact of this effect is small as the average conductivity of the displaced inner compartment deviated only 2-7% compared to the conductivity value of the centrally located compartment. The tested off-center positions cover the range of positions we expect for the tumors of our interest, i.e. cervical, bladder and prostate tumors. This indicates that the conductivity reconstruction is reliable for these tumor groups.

As short scan times are desirable in the clinics, the simplified EPT reconstruction using phase-only data was considered in this work. Earlier studies in the brain (23,24) have shown that conductivity reconstruction at 1.5T and 3T yields better results compared to 7T due to the lower phase error and lower noise level at 1.5T and 3T. In this study, it was demonstrated that phase only EPT reconstruction yields an overestimation of the conductivity values for which it can be accounted for. In (31) an overestimation of 10% was observed for most tissue types for phase-only reconstruction based on simulations at 1.5T. Based on the phantom experiments presented in this work, an overestimation between 1% and 25% was observed for phase-only reconstruction compared to probe measurements. Furthermore, in vivo conductivity reconstruction based on phase-only measurements (Fig 7p) does not suffer from asymmetries that are observed in Figure 7m. The conductivity error of the phase-only reconstruction, introduced due to omission of the second term of Eq.(2), cannot directly be related to the \( |B^\dagger_1| \) map only as the error is related to the inner product of gradients in \( |B^\dagger_1| \) and \( \phi^\pm \). The asymmetries observed in Figure 7m are
introduced due to the inner product of $\nabla|B_1^+|$ and $\nabla\phi^\pm$ where the latter one is determined by $B_1^-$ as well.

In vivo conductivity maps of the pelvis are, however, more challenging. This is due to a combination of factors. First of all, the $B_1^+$ amplitude and especially the phase measurement can be easily corrupted by bowel and respiratory motion. In the cervix and prostate region of the pelvis it was found that respiratory motion is not really problematic with regard to phase measurements. Peristaltic motion was found to have more impact. We addressed this issue by using an agent (Buscopan®) that minimizes peristaltic motion which is a common practice in oncologic MR imaging of the pelvis.

A more fundamental problem degrading the accuracy, is the corrupted conductivity estimates around tissue boundaries which are numerous due to the heterogeneous anatomy of the pelvis. This error is caused by piece-wise media assumption in the Helmholtz based EPT reconstruction method and the numerical implementation of the Laplacian (16,23). Current EPT reconstruction schemes assume piece-wise constant dielectric properties, however, this assumption does not hold at tissue boundaries. This results in a corrupted conductivity reconstruction at the tissue boundary (Fig. 3) or complete blurring in case of small tissue types (e.g. blood vessels) as observed in Figure 6 (1st column). Additionally, the kernel-based implementation of the Laplacian may also introduce boundary errors as it projects for the local $B_1^+$ curvature estimation spatial information of one tissue into its adjacent tissue. Also the intrinsic sensitivity of the Laplacian to noisy measured data affects the quality of the reconstructed conductivity maps based on measurements. Boundary errors regarding the Laplacian may be reduced by considering backward and forward differentiation or by adapting the kernel-size near boundaries. A recent study (39) has introduced a new approach based on Contrast Source Inversion method. This approach is free of assumptions regarding the piece-wise regions and is based on integral representations of the electromagnetic field, avoiding derivatives of $B_1^+$ fields. This method offers improvements of EPT results regarding conductivity reconstruction near tissue boundaries.

As shown in this study, the transceive phase assumption is applicable at 3T for the human pelvis. However, simulation results (Fig. 4a and 7j) show that a slight improvement may be achieved if the $B_1^+$ phase can be determined. Recent studies (40–43) avoid the transceive phase assumption by using multiple independent transmit/receive channels and open up possibilities for EPT reconstruction free of assumptions regarding the $B_1^+$ phase. Modern clinical 3T scanners are often equipped with 2 transmit channels for RF shimming purposes and thus this new methodology might also be introduced here. However, to fully utilize these methods more than two transmit channels are preferred as high SNR might be required for the two-channel systems. Particularly when the aim is to reconstruct the conductivity of the whole anatomy, this method might be valuable. For central locations, the added value is, however, limited.

Conductivity reconstruction as presented in this work, has various applications besides Hyperthermia Treatment Planning. Due to its ability to reconstruct a wide range
Feasibility of EPT of pelvic tumors

of conductivity values, it can be applied for tumor detection and characterization (3). Based on previous studies tumors may have elevated conductivity values compared to the surrounding healthy tissue. A further application would be the use of reconstructed conductivity values for RF safety purposes in MRI. However, to fully utilize EPT for MR safety and HTP in the complete pelvis region, the reconstruction of the whole pelvis region should be accomplished and the error margins at tissue boundaries should be reduced. Also, the reconstruction of inter-tissue conductivity variation might further improve RF safety assessment, and should be subject to further research.

3.5 Conclusion

This study demonstrates the feasibility of EPT to measure quantitatively the electric conductivity of centrally located tumors in a pelvic-sized phantom and human pelvis with a standard MR system and MR sequences. A good quantitative agreement was found between the spatially-averaged conductivity values and probe measurements for a wide range of \( \sigma \)-values and for off-axis located spherical compartment. The phase-only conductivity mapping shows a systematic overestimation of the true conductivity values. As most pelvic tumours are located in the central region of the pelvis these results can be exploited in Hyperthermia Treatment Planning systems. In vivo measurements illustrated the feasibility of EPT to reconstruct the conductivity of tumors in the pelvic region, however, the reconstruction of \( \sigma \)-map of the whole pelvic region should be subject to further research.

Acknowledgments

This study was supported by grant UVA 2010 4660 of the Dutch Cancer Society.

References


