The analysis of prostate images is one of the most complex tasks in medical images interpretation. It is sometimes very difficult to detect early prostate cancer using currently available diagnostic methods. But the examination based on perfusion computed tomography (p-CT) may avoid such problems even in particularly difficult cases. However, the lack of computational methods useful in the interpretation of perfusion prostate images makes it unreliable because the diagnosis depends mainly on the doctor’s individual opinion and experience. In this paper some methods of automatic analysis of prostate perfusion tomographic images are presented and discussed. Some of the presented methods are adopted from papers of other researchers, and some are elaborated by the authors. This presentation of the method and algorithms is important, but it is not the master scope of the paper. The main purpose of this study is computational (deterministic and independent) verification of the usefulness of the p-CT technique in a specific case. It shows that it is possible to find computationally attainable properties of p-CT images which allow pointing out the cancerous lesion and can be used in computer aided medical diagnosis.

Keywords: prostate cancer, perfusion computed tomography, medical image analysis, pattern recognition.

1. Introduction

Prostate cancer (PCa) is one of the most common malignancies among men (ACS, 2009; NCR, 2009). In the last years there has still been observed a growth in the number of registered cases. And although it is partially connected with better and better diagnostic methods and increased knowledge among patients (resulting in better detectability of this type of cancer), there is no doubt that PCa is a serious medical and social problem.

Early detection of PCa is a key to survival. Unfortunately, routine medical tests like measuring blood concentration of prostate specific antigen (PSA), digital rectal examination (DRE), transrectal ultrasound (TRUS), and biopsy often fail (Hricak et al., 2007; Roscigno et al., 2004; Selley et al., 1997). For example, on TRUS, cancer lesions can be hypoechoic, hyperechoic or even isoechoic (Daehnert et al., 1986; Norberg et al., 1997; Sudol-Szopińska and Szopiński, 2005). In view of this, there is an obvious need for other diagnostic methods which could manage this problem in some cases which are too difficult for standard (above mentioned) methods.

There are many studies of new techniques which could address this problem, including, for example, the EPCA test (Bradford et al., 2006; Leman et al., 2007). Perfusion computed tomography (p-CT) is also one of these methods (still under investigation). This method allows evaluating the parameters of perfusion such as blood flow (BF), blood volume (BV), mean transit time (MTT), permeability surface (PS) in specified areas of prostate (ROI—region of interest) (Cenic et al., 2000; Wintermark et al., 2001).
Nowadays the p-CT examination is used mainly in the diagnosis of brain acute stroke (Miles and Griffiths, 2003; Hartel et al., 2006; Hoefnner et al., 2004; Rosenberg et al., 2004), but the usefulness of this method has also been tested on other organs (Miles and Griffiths, 2003; Blomley et al., 1993; Dugdale and Miles, 1999; Dziubinska et al., 2006; Fukuya et al., 1995; Groell et al., 2001; Sahani et al., 2005; Wolfkiel et al., 1987; Zhang and Kono, 1997), including prostate (Henderson et al., 2003; Ives et al., 2005; Luczyńska et al., 2008; Prando and Wallace, 2000). Its application to detecting cancerous lesions is based on documented evidence of the creation of new blood vessels in tumor (angiogenesis) (Charlesworth and Harris, 2006; Miles, 1999; 2002). Although prostate is not highly vascularized, it is supposed that p-CT can indicate these suspicious areas also in this gland.

The purpose of this study is computational verification of usefulness of the p-CT technique in a specific case, described in the paper (Łuczyńska et al., 2006). In that case, diagnostics correctly pointed cancerous lesions on the p-CT image, while on TRUS there were no visible suspicious regions. However, that indication was founded only on visual assessment, so it can be considered underterministic and unreliable.

2. Images

A 60-year-old patient was examined at the Oncology Center in Cracow because of an increasing PSA level. The p-CT examination was performed with a 16-slice CT scanner (GE Ligh Speed Advantage). The perfusion level was measured during repeated scans of the minor pelvis at 120 kVp and 200 mAs. The scans were started about 10 s after administering of 50 ml of non-ionic contrast medium (370 mgI/ml) at the rate of 5 ml/s and lasted 50 s. The total width of the diagnosed area was 20 mm.

Parametric maps (BF, BV, MTT and PS) were drawn using the CT Perfusion 3 application on the Advantage Workstation at three levels (conventionally base, middle and apex) of the gland.

In order to perform computational analysis, only the area of prostate was selected from the acquired images. The images, originally coded with pseudocolor, where blue symbolizes the area with minimal and red—with maximal perfusion, were transformed into a 31-tone grayscale using the LUT table (Tadeusiewicz and Korocho, 1997), where 0 means maximal visible perfusion (red area in pseudocolor) and 30—no perfusion. (Fig. 1)

Figure 2 presents parametric maps of the prostate (coded with pseudocolor) at the level at which pathological lesions were confirmed (Fig. 3). In this work only the image of Fig. 2(a), which represents the parameter BF, is selected for further analysis.

3. Co-occurrence matrices

For automatic description of the texture of particular regions on the analyzed p-CT image, the so-called co-occurrence matrices (Haralick et al., 1973) were selected. There are many other texture analysis methods, but these are most universal and their potential is greatest.

Let \( I : \mathbb{Z}^2 \rightarrow D \rightarrow G = \{1, \ldots, N_g\} \) (where \( \mathbb{Z} \) denotes set of integers) be a two-dimensional discrete image with \( N_g \) gray levels. For the given image \( I \), we define the co-occurrence matrix (GLCM):

\[
P_0(i, j|d, \theta) = \# \{ k, l \in D : I(k) = i, \, I(l) = j, \, ||k-l|| = d, \, \angle(k-l) = \theta \}
\]

or, in a normalized version,

\[
P(i, j|d, \theta) = \frac{\# \{ k, l \in D : I(k) = i, \, I(l) = j, \, ||k-l|| = d, \, \angle(k-l) = \theta \}}{\# \{ m, n \in D : ||m-n|| = d, \, \angle(m-n) = \theta \}}.
\]

where \( i, j \in G \) stand for gray levels of points \( k \) and \( l \), respectively, \( \angle(k-l) \) is the angle between vector \( \overrightarrow{kl} \) and axis \( 0X \). \( d \) represents the distance between \( k \) and \( l \), \( \theta \) is the direction of co-occurrence, \( \#X \) represents the power (number of elements) of set \( X \).

Fig. 1. Pseudocolor (a), grayscale after transformation (b). The arrow shows a rise in the perfusion values.

Fig. 2. p-CT images of the prostate: blood flow (BF) (a), blood volume (BV) (b), mean transit time (MTT) (c), permeability surface (PS) (d).

Fig. 3. Analyzed image (a) and cancerous area (b)—shown in black.
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Table 1. Coefficients of GLCM.

<table>
<thead>
<tr>
<th>no.</th>
<th>name</th>
<th>abbr.</th>
<th>value</th>
</tr>
</thead>
<tbody>
<tr>
<td>f_1</td>
<td>energy</td>
<td>ENE</td>
<td>( f_1 = \sum_{i,j} P(i,j)^2 )</td>
</tr>
<tr>
<td>f_2</td>
<td>entropy</td>
<td>ENT</td>
<td>( f_2 = -\sum_{i,j} P(i,j) \log P(i,j) )</td>
</tr>
<tr>
<td>f_3</td>
<td>homogeneity</td>
<td>IDM</td>
<td>( f_3 = \frac{1}{1 + (i - j)^2} )</td>
</tr>
<tr>
<td>f_4</td>
<td>inertia</td>
<td>CON</td>
<td>( f_4 = \sum_{i,j} (i - j)^2 P(i,j) )</td>
</tr>
<tr>
<td>f_5</td>
<td>correlation</td>
<td>COR</td>
<td>( f_5 = -\sum_{i,j} \frac{(i - \mu_x)(j - \mu_y)}{\sigma_x \sigma_y} P(i,j) )</td>
</tr>
<tr>
<td>f_6</td>
<td>variance</td>
<td>VAR</td>
<td>( f_6 = \sum_{i,j} (i + j - \mu_x - \mu_y)^2 P(i,j) )</td>
</tr>
<tr>
<td>f_7</td>
<td>shade</td>
<td>SHA</td>
<td>( f_7 = \sum_{i,j} (i + j - \mu_x - \mu_y)^3 P(i,j) )</td>
</tr>
<tr>
<td>f_8</td>
<td>prominence</td>
<td>PRO</td>
<td>( f_8 = \sum_{i,j} (i + j - \mu_x - \mu_y)^4 P(i,j) )</td>
</tr>
<tr>
<td>f_9</td>
<td>sum average</td>
<td>SA</td>
<td>( f_9 = \frac{2N_g}{\sum_{i,j} \sigma_{i,j}} )</td>
</tr>
<tr>
<td>f_10</td>
<td>sum entropy</td>
<td>SE</td>
<td>( f_{10} = -\sum_{i,j} P_{x+y}(i) \log P_{x+y}(i) )</td>
</tr>
<tr>
<td>f_11</td>
<td>sum variance</td>
<td>SV</td>
<td>( f_{11} = -\sum_{i,j} (i - f_2)^2 P_{x+y}(i) )</td>
</tr>
<tr>
<td>f_12</td>
<td>difference average</td>
<td>DA</td>
<td>( f_{12} = \sum_{i,j} \sigma_{i,j} )</td>
</tr>
<tr>
<td>f_13</td>
<td>difference entropy</td>
<td>DE</td>
<td>( f_{13} = -\sum_{i,j} P_{x+y}(i) \log P_{x-y}(i) )</td>
</tr>
<tr>
<td>f_14</td>
<td>difference variance</td>
<td>DV</td>
<td>( f_{14} = -\sum_{i,j} (i - f_2)^2 P_{x-y}(i) )</td>
</tr>
<tr>
<td>f_15</td>
<td>information measure</td>
<td>IMCI</td>
<td>( f_{15} = \frac{f_2 - \frac{1}{\max(HX, HY)}}{\max(HX, HY)} )</td>
</tr>
<tr>
<td>f_16</td>
<td>coefficient of variation</td>
<td>COV</td>
<td>( f_{16} = \frac{\sigma P(i,j)}{\mu P(i,j)} )</td>
</tr>
<tr>
<td>f_17</td>
<td>peak transition probability</td>
<td>MAX</td>
<td>( f_{17} = \max(P(i,j)) )</td>
</tr>
<tr>
<td>f_18</td>
<td>diagonal variance</td>
<td>DIAV</td>
<td>( f_{18} = \sigma^2(P(i,j)) )</td>
</tr>
<tr>
<td>f_19</td>
<td>diagonal moment</td>
<td>DIAM</td>
<td>( f_{19} = \sum_{i,j} \left( \frac{1}{\sigma_{i,j}} - 1 \right)^2 )</td>
</tr>
<tr>
<td>f_20</td>
<td>second diagonal moment</td>
<td>DSM</td>
<td>( f_{20} = \sum_{i,j} \frac{1}{\sigma_{i,j}} \left( \frac{i - j}{P(i,j)} \right)^2 )</td>
</tr>
<tr>
<td>f_21</td>
<td>triangular symmetry</td>
<td>TRS</td>
<td>( f_{21} = \left</td>
</tr>
</tbody>
</table>

Notation

\[
\begin{align*}
\mu_x &= \sum_i \sum_j P(i,j), \\
\mu_y &= \sum_j \sum_i P(i,j), \\
\sigma_x &= \sum_i (i - \mu_x)^2 \sum_j P(i,j), \\
\sigma_y &= \sum_j (j - \mu_y)^2 \sum_i P(i,j), \\
P_x(i) &= \sum_j P(i,j), \\
P_y(j) &= \sum_i P(i,j), \\
P_{x+y}(i,j) &= \sum_{i,j} P(i,j), \\
P_{x-y}(i,j) &= \sum_{i,j} P(i,j), \\
HX &= \text{entropy } P_x(i), \\
HY &= \text{entropy } P_y(j), \\
HX \cdot HY &= -\sum_{i,j} P(i,j) \log(P_x(i)P_y(j))
\end{align*}
\]
The GLCM allows us to evaluate a number of coefficients, which characterize the textures of the analyzed image. Table 1 shows the list of 21 coefficients used in our study.

4. Results

For the given image of Fig. 3(a) transformed to grayscale we evaluated the first-order statistics calculated directly from the image histogram (Table 2). The mean in a healthy area is smaller than in a cancerous one but the variance is very high in both cases. Therefore, the analysis based only on the first-order statistics of the ROI considered (see below) may not be sufficient (Table 3, Fig. 6).

The ROIs covering the analyzed image were rectangular in shape, 10 pixels wide and 20 pixels high. Each consecutive ROI was selected 10 pixels apart the previous one. Those where less than half of the pixels covered the area of prostate were missed. Each ROI was classified according to the pattern shown in Fig. 3(b). There were 88 ROIs at all: 82 healthy and six cancerous (Fig. 7). For each ROI, normalized GLCM matrices (see Eqn. (2)) and coefficients were evaluated.

There were calculated 21 coefficients (Table 1) for each GLCM characterized by distance \( d \) in the range from 1 to 9, and angle \( \theta \) with values 0\(^\circ\), 45\(^\circ\), 90\(^\circ\), 135\(^\circ\), and also \( d \) in the range from 10 to 19 and \( \theta = 90^\circ \). So it was the 966-dimensional feature space. The resulting values for each feature were analyzed in order to eliminate outliers and normalized. The distribution of each feature was equalized using the ladder of powers method (Tukey, 1977; Velleman and Hoaglin, 1981) (see Eqn. 3) with \( \gamma \in (0, 2] \).

\[
\text{error}(\gamma) = \sum_{c=1,2} \left( \int_{x} \left[ \text{cdf}(x^\gamma) - \Phi(x^\gamma, \text{var}(x^\gamma)) \right]^2 \right),
\]

where \( c = \{1, 2\} \) represents classification, \( \text{cdf}(x^\gamma), \overline{x^\gamma}, \text{var}(x^\gamma) \) stand for the distribution function, mean and variance of empirical distribution for class \( c \), respectively, \( \Phi(\mu, \sigma^2) \) is a normal distribution function with mean \( \mu \) and variance \( \sigma^2 \).

We were looking for \( \gamma_{\text{opt}} \) which minimizes the function \( \text{error}(\gamma) \):

\[
\gamma_{\text{opt}} = \min_{\gamma} \text{error}(\gamma).
\]
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Table 2. First-order statistics of the analysed image.

<table>
<thead>
<tr>
<th>parameter</th>
<th>mean</th>
<th>median</th>
<th>variance</th>
<th>std.dev.</th>
<th>skewness</th>
<th>curtosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>all image</td>
<td>5.72</td>
<td>4</td>
<td>33.98</td>
<td>5.83</td>
<td>1.63</td>
<td>2.88</td>
</tr>
<tr>
<td>healthy area</td>
<td>5.20</td>
<td>4</td>
<td>26.15</td>
<td>5.11</td>
<td>1.52</td>
<td>2.51</td>
</tr>
<tr>
<td>cancerous area</td>
<td>12.47</td>
<td>11</td>
<td>85.21</td>
<td>9.23</td>
<td>0.47</td>
<td>−0.92</td>
</tr>
</tbody>
</table>

Features where $\text{error}(\gamma_{\text{opt}}) \geq 1$ were excluded from further analysis. For each of the remaining features, the Bhattacharyya measure (Bhattacharyya, 1943) was used for the normal distribution:

$$J = \frac{1}{4} \frac{(\mu_1 - \mu_2)^2}{\sigma_1^2 + \sigma_2^2} + \frac{1}{2} \ln \left( \frac{\sigma_1^2 + \sigma_2^2}{2\sigma_1\sigma_2} \right),$$

(5)

where $\mu_1, \mu_2$ are means, $\sigma_1, \sigma_2$ are standard deviations for Classes 1 and 2, respectively. Below, in Table 2 we present a list of the best discriminating properties. As is shown, the best results were produced for the diagonal moment ($f_19$) and various $d$ and $\theta$. It should be noted that diagonal directions $\theta = 45^\circ$ and $\theta = 135^\circ$ did not occur in any of the best ten features.

As can be remarked, the above-mentioned consideration is limited to the indication of a single individually best discriminating feature (Fig. 8). It should be observed that, in spite of these limitations, it is possible to indicate such features which individually have the ability to distinguish a healthy and a cancerous area (Fig. 9). However, it is not a universal rule—even for features with a large distance between classes, sometimes these areas cannot be separated (Fig. 10). In such cases it can be helpful to increase the dimension of the feature space (Fig. 11).

5. Conclusion

In this paper it was shown that it is possible to select such parameters of an image which are deterministic and independent of a personal assessment. Our results confirm the usefulness of the p-CT method applied to PCa diagnosis in the analyzed case. Of course, it is obvious that only one case cannot be generalized, but in this study the potential of this method can be seen.

At the Oncology Center in Cracow the p-CT method is used to examine other patients. Thanks to that it will be possible to verify the usefulness of the proposed algorithm. In further work the authors will also expand research to other perfusion parameters to determine the effectiveness of each one.

References


Table 4. List of ten features with the best discriminant power.

<table>
<thead>
<tr>
<th>displacement $d$</th>
<th>angle $\theta$</th>
<th>coefficient</th>
<th>Bhattacharyya measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>0</td>
<td>diagonal moment ($f_{19}$)</td>
<td>2.494145</td>
</tr>
<tr>
<td>10</td>
<td>90</td>
<td>diagonal moment ($f_{19}$)</td>
<td>2.441980</td>
</tr>
<tr>
<td>1</td>
<td>90</td>
<td>triangular symmetry ($f_{21}$)</td>
<td>2.181827</td>
</tr>
<tr>
<td>3</td>
<td>90</td>
<td>prominence ($f_{3}$)</td>
<td>2.074908</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>variance ($f_{4}$)</td>
<td>2.051128</td>
</tr>
<tr>
<td>6</td>
<td>90</td>
<td>sum entropy ($f_{10}$)</td>
<td>1.962097</td>
</tr>
<tr>
<td>4</td>
<td>90</td>
<td>prominence ($f_{3}$)</td>
<td>1.843247</td>
</tr>
<tr>
<td>11</td>
<td>90</td>
<td>diagonal moment ($f_{19}$)</td>
<td>1.839980</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>sum entropy ($f_{10}$)</td>
<td>1.836315</td>
</tr>
</tbody>
</table>


Fig. 8. Analyzed image (a), illustration of the best discriminating features (b–k), and of the feature with no discriminant power (l).

d = 8, \theta = 0^\circ, f_{19} (b), d = 10, \theta = 90^\circ, f_{19} (c), d = 1, \theta = 0^\circ, f_{21} (d), d = 3, \theta = 90^\circ, f_8 (e), d = 3, \theta = 0^\circ, f_6 (f),

\quad d = 6, \theta = 90^\circ, f_{10} (g), d = 11, \theta = 90^\circ, f_{19} (h), d = 4, \theta = 90^\circ, f_8 (i), d = 11, \theta = 90^\circ, f_{20} (j), d = 4, \theta = 0^\circ, f_{10} (k),

\quad d = 8, \theta = 45^\circ, f_{15} (l).


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