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A novel approach for quantification of time–intensity curves in a DCE-MRI image series with an application to prostate cancer

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ABSTRACT

This paper considers the problem of an automatic quantification of DCE-MRI curve shape patterns. In particular, the semi-quantitative approach which classifies DCE time–intensity curves into clusters representing the tree main shape patterns is proposed. The approach combines heuristic rules with the naive Bayes classifier. In particular, the descriptive parameters are firstly derived from pixel-by-pixel analysis of the DCE time intensity curves and then used to recognise the curves which without a doubt represent the three main shape patterns. These curves are next used to train the naive Bayes classifier intended to classify the remaining curves within the dataset. Results of applying the proposed approach to the DCE-MRI scans of patients with prostate cancer are presented and discussed. Additionally, the overall performance of the approach is estimated through the comparison with the ground truth results provided by the expert.

1. Introduction

Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) is an extension of magnetic resonance technique, intended to measure changes of contrast agent concentration within tissues over the time. In particular, it consists of a sequence of MRI acquisitions performed before, during and after the injection of the contrast bolus. The change in image intensity in each time sequence represents the change in contrast concentration. Since the concentration changes exhibit different patterns depending on physiological tissue characteristic, recently DCE-MRI have been more and more frequently considered by the oncologists and radiologists as a promising method for cancer detection, diagnosis and staging. By the analysis of DCE curve shape patterns it is possible to non-invasively distinguish healthy tissue from the cancerous one, as well as to discriminate between malignant and benign cancerous changes [1,2].

So far, DCE-MRI has been widely used for diagnosis of breast lesions [1–3]. However, recently this technique has also been applied to improve specificity of MRI in characterizing cancerous lesions of different organs, e.g. liver [4], knee joints [5], prostate [6] or rectum [7]. Therefore, the development of reliable methods for DCE time–intensity curves (TIC) assessment is one of the key issues in DCE image analysis.

The reported methods of DCE curve analysis can be qualified into three general categories, namely: qualitative methods, semi-quantitative methods and quantitative methods [8].

The qualitative methods are the most common and are simply based on visual inspection. In such a case, the analysis and quantification of the DCE curve pattern is performed visually, based the time–intensity curves (TIC) plotted using the dedicated computer aided diagnosis (CAD) software. This kind of the analysis is usually limited to the region of interest (ROI) indicated manually in a suspicious region. Additionally, the TICs may be obtained for single pixels or averaged over the ROI. The main drawback of this method of analysis is the lack of quantitative parameters describing the underlying tissue characteristics. As a result, the intra-observer variability in the assessment of curve pattern can be observed, especially in the case of patterns demonstrating atypical configurations. Secondly, averaging of the signal over the region of interest may ignore or diminish the influence of the small foci of the disease.

The recent research on DCE-MRI signal curves include mainly the development of semi-quantitative and quantitative methods, which allow to overcome some drawbacks of the qualitative methods [9].

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The quantitative approaches to DCE-MRI curve analysis aim at extracting meaningful quantitative parameters that directly reflect blood flow and physiological characteristics of the underlying tissues. This is performed using pharmacokinetic modelling techniques, i.e. by fitting mathematical models describing the changes of the contrast agent into DCE curves [10,11]. Several pharmacokinetic models exist, however the most commonly used is the model proposed by Tofts [12,11], which considers the blood plasma and the extracellular extra-vascular space as two compartments. Models proposed by Brix [13] and Larsson [14] are also popular.

Although the quantitative approaches to DCE signal analysis are the closest to the underlying tissue physiology, they exhibit a number of drawbacks. First of all, these methods are computationally demanding. Some efforts for reducing their computational complexity have already been made [15], however their usage in the case of high resolution volumetric images is still limited. Additionally, modelling is often a source of uncertainty, since different models can provide significantly different values of the same physiological parameters. What is more, these methods do not make use of model assumptions or non-linear fitting. As a result, for some cases the fitting algorithm may appear unstable. Additionally, to perform pharmacokinetic modelling, the knowledge about the arterial input function (AIF) is usually required but not always available or ambiguous. Since AIF varies depending on a region, assuming its uniformity is another source of errors. There are some models reported in the literature which do not require an AIF [16], these however are in minority.

The last group i.e. the semi-quantitative approaches are an intermediate solution between the quantitative and qualitative methods. They do not take advantage from the pharmacokinetic analysis, but try to relate the curve shape pattern to physiological findings. These methods are based on descriptive parameters which reproduce main features of an expected curve directly derived from DCE TICs. Firstly, the pixel-by-pixel analysis of the curves is performed in order to extract parameters which include signal wash-in slope, signal wash-out slope, time to peak, maximal signal enhancement or initial area under the curve [17]. Then using the heuristic rules with respect to these parameters the TICs are qualified into the main shape patterns. Most of the existing approaches qualify the curves into the three groups representing shape patterns, however some authors have proposed to distinguish additional types [18]. Since semi-quantitative methods for curve analysis do not require curve fitting, they are usually more robust, than methods based on the pharmacokinetic modelling. However, since they require pixel-by-pixel curve processing, they may be sensitive to intensity variations (noise), hardware settings, contrast parameters, etc. Additionally, heuristic rules are not able to handle curves which demonstrate atypical shape patterns.

A few approaches based on the unsupervised clustering have also been proposed [19]. These are used directly on DCE-MRI signal curves either by considering them as vectors of intensities or as vectors of features derived from TICs. Supervised clustering methods require the correct number of clusters to be given in advance. This is a serious limitation, since it is *a priori* unknown how many clusters should be distinguished.

To the best of the author's knowledge, supervised clustering approaches to DCE-MRI curve pattern recognition have not been reported, since they require the expert knowledge in the classifier training phase. Especially, in the considered problem the expert should manually classify the DCE TICs within the training set into the three categories. This is however difficult and time consuming. Additionally, the results may differ depending on the expert.

The approach introduced in this paper is a step towards introducing supervised clustering methods into the quantitative analysis and automatic recognition of DCE time–intensity curve shape patterns. It combines heuristic models incorporated into a training phase with a naive Bayes classifier used for TIC shape pattern recognition. The approach was developed with the aim of application in the prostate cancer assessment and thus its performance is presented and assessed using the DCE-MRI image series of patients with prostate cancer provided by the Initiative for Collaborative Computer Vision Benchmarking (I2CVB) [20]. However, the method is general and its application is not limited only to the prostate cancer.

The remainder of this paper is organised as follows. First, in Section 2 the three main DCE time–intensity curve shape patterns are briefly characterised. This is followed in Section 3 by the description of the DCE-MRI dataset used in this study. The proposed approach is described in details in Section 4 and followed by the presentation, assessment and discussion of the results provided in Section 5. Finally, Section 6 concludes the paper.

2. DCE curve shape patterns

The shape of the DCE time intensity curve typically falls into one of the three general categories (types) [21].

The first curve shape pattern (Type 1) presents slow progressive contrast enhancement (intensity increase) during the acquisition time. Usually, the signal does not reach intensity maximum during the image acquisition period which is a suggestive of a healthy tissue.

Type 2 is assigned to curves which present stable initial contrast uptake (increase of image intensity) followed by a plateau i.e. the phase of a relatively constant signal intensity. This type of curve correspond with an intermediate probability for malignancy.

Finally, Type 3 curves exhibit fast initial contrast (signal intensity) enhancement followed by a quick gradual wash out after the peak signal intensity is achieved during the initial phase. The third type of DCE curve shape pattern is indicative of malignancy.

The representative curves for each of the three categories mentioned above are sketched in Fig. 4.

3. Input data

The research described in this paper was performed using the benchmark multi-parametric MRI (mp-MRI) images of prostate provided by the Initiative for Collaborative Computer Vision Benchmarking (I2CVB) [20]. In particular, the dataset *dijon* acquired by a 3.0 Tesla Siemens Magnetom Trio TIM scanner was considered. The dataset is composed of a total of 19 patients including 17 subjects with diagnosed prostate cancer (CaP) and two healthy ones. In all the considered patients the diagnosis was proven by a guided-biopsy performed aside of the MRI examinations. Each MRI scan included 5 different modalities (T_2-weighted MRI, dynamic contrast enhanced MRI, diffusion weighted imaging MRI, magnetic resonance spectroscopic imaging and apparent diffusion coefficient maps) of which dynamic contrast enhanced (DCE) MRI time series were used. These were obtained after application of gadolinium contrast in the amount of 15 ml. Each DCE-MRI time series consisted of 40 acquisitions (frames) of the resolution $200 \times 256 \times 16$ voxels each (16 slices of spatial resolution 200×256 pixels), pixel spacing of $1.09 \times 1.09\ \mathrm{mm}^2$ and slice thickness equal 3.5 mm. The duration of a resulting dilution curve ranged from 265 to 318 s (with the average duration equal to 259 s and median duration equal to 265 s). Additionally, for each patient the ground truth segmentations of the cancerous region were provided for each modality, including the considered DCE-MRI sequences. According to the description of the dataset, the ground truths were prepared manually by an experienced radiologist (Fig. 1).