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Deformable Models and Optimal Mass Transportation for Processing of DCE-MRI 2D Images

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Abstract: Post-contrastographic Dynamic Contrast Enhancement (DCE) is a consolidated MRI technique to perform non-invasive analysis via Imaging. The dynamics perfusion of specific drugs, named Contrast Agents (CA), allows to highlight anomalies in tissues, since the vascular substrate is differently developed (hypervascularized) for diseases compared with healthy parenchyma. The goodness of the analysis procedure influences the inferred diagnosis: the more objective the analysis, the more accurate the prognosis and the therapies follow-up. Deformations and displacements affect organs and soft tissues and their correction is challenging for DCE analysis; the complexity lies also on artefacts of image registration process because of the backscattered image signal intensity varies over time due to the diffusion/perfusion phenomenon induced by the CA injection. In this work we present a combined approach based on the Active Contours framework and on the Optimal Mass Transportation for the automatic depicting and tracking of deformable objects. Active Contours provide the automatical contour's depiction of a deformable object by minimizing an energy cost functional; Optimal Mass Transportation allows to tracking a deformable object by minimizing the (object's) transport cost under the (object) mass conservation principle. We applied these methodologies to post-contrastographic DCE MR images' series and we are going to show the improvement in the goodness of DCE analysis compared with results gathered with other tracking strategies.

Keywords: Active Contours, Optimal Mass Transportation, Post-Contrastographic DCE, MR Imaging, Kernel Tracking, Contour Tracking.

1. INTRODUCTION

Clinical practice, investigations and diagnostic procedures use Imaging; nowadays, non-invasive techniques, such as Magnetic Resonance Imaging (MRI), support medical research and diagnosis [9], [14], [15]. Post Contrastographic Dynamic Contrast Enhancement (DCE) procedure, based upon the assessment of the enhanced backscattered signal intensity measurements over time, highlights suspicious lesions [4], [8], [21] [23], when a specific drug, called Contrast Agent (CA) perfuses into regions with an abnormal vascular network, showing tissues anomalies and/or necrosis. Whatever the investigated region, the DCE technique assesses the Contrast Enhancement curve (of tissues) over time and its parameters and provides useful information for making a diagnosis [12]. The precision within the region detection is crucial: the more detailed, the more accurate the DCE analysis and the subsequent inferred diagnosis.

Object depiction and tracking, in an environment, is a challenging task. The Tracking Motion problem can be stated as the problem of estimating the trajectory of said object - either rigid or deformable - inside an image series; this is not a trivial task because of the complexity of the form to be depicted and tracked, the unknown trajectory followed and the noise of the image. Solutions to this problem can be addressed in answering the following questions:

(1) Which is the best representation of the object?
Objects classification relies on intrinsic features: shape or geometric configuration, or on extrinsic characteristics: intensity, colour, brightness, etc; [25];
(2) How to model the contour of the object?
The used approaches are kernel, silhouette and/or contour tracking [25];
(3) Which are the best features to help track an object?
Colour, intensities, edges, optical flows, textures, densities address this issue [2], [25].

In this work we face the Contour Tracking Motion issue for improving the DCE analysis, by combining techniques for the automatic depiction of deformable objects, and algorithms for the tracking of those objects through different images acquisition over time. We applied Active Contours (AC) framework, based on the dynamics of elastic elements given by forces and constraints, for the best approximation of the object outline [2], [6], [11], [13], and the Optimal Mass Transportation (OMT), based on the mass conservation principle, to perform the Contour Tracking Motion [1], [7], [10], [22], [24] of a deformable object in a image time series.

We report the comparison of different analysis methods for showing how differs the Contrast Enhancement curve among those obtained without, and partial, application of corrective actions; moreover we compared the timing cost of different tracking techniques for choosing the best compromise between the goodness of analysis and the computational burden. The aim of this study is to decipher improvements in the OMT-based corrections: are these more appreciable and effective in smaller object even though the timing cost is greater?

2. METHODS AND MODELS

The tracking motion problem can be described in the following terms: it is given a sequence of 2-D different (subsequent) temporal or spatial frames; these frames contain the object to be tracked plus the environment and some noise. The problem can be stated as follows:

(1) Identify the object to be tracked, using parameters like the brightness and/or the colors of pixels to depict the object contour;
(2) Estimate the continuous-time trajectory of the object in $\mathbb{R}^2$, i.e. describe the trajectory of each point forming the object;
(3) On the basis of the previous point, describe the association of each pixel belonging to a specific frame into one or more pixels of the following one.

Deformable models to represent the object's contour, and Optimal Mass Transportation to describe object's trajectory, provide valuable tools to anwer these issues.

2.1 Deformable Models for Object's Identification in Biomedical Images

Active Contours framework, based on deformable models, mates well with the amorphous, nonrigid boundaries found in many biomedical applications. The contour's depiction by the AC framework relies on the idea of a deformable model, that evolves independently adapting to the object variations by minimizing a cost functional [2], [6], [11], [13]. A physicist might interpret the deformable contours as a set of elastic elements able to change their position due to the application of forces: by minimizing the energy functional, it is possible to reach an equilibrium position associated with the best object edges configuration. A mathematical representation of an AC is a parametric curve (or snake):

$$V(s) = [X(s), Y(s)] \tag{1}$$

where vectors $X(s)$ and $Y(s)$ collect the contour's coordinates, generally obtained using B-Splines functions [5], that allow depicting a continuous and smoothing parameterized contour. To each AC it is associated an energy function:

$$\begin{aligned} E_{snake} = & \int_0^1 \frac{1}{2}\left[\alpha\left(\left|\frac{dX}{ds}\right|^2 + \left|\frac{dY}{ds}\right|^2\right)\right] ds + \\ & + \int_0^1 \frac{1}{2}\left[\beta\left(\left|\frac{d^2X}{ds^2}\right|^2 + \left|\frac{d^2Y}{ds^2}\right|^2\right)\right] ds + \\ & - \kappa \int_0^1 \left(f\,[X(s), Y(s)]\right) ds \end{aligned} \tag{2}$$

where the first two terms form the Internal Energy, and are: the Stretching Energy (likewise, the tension) that prevents the contour from getting stretched, and the Bending Energy (also known as rigidity) that prevents the bending of the snake; getting greater the rigidity allows making the curve as regular as possible, by maximizing the contour internal angles [20].The third term refers to the External Energy where:

$$f(X(s), Y(s)) = |\nabla\,(G_\sigma(x,y) \otimes I(x,y))|, \tag{3}$$

refers to the image (I) gradient previously convolved with a gaussian smoothing filter, whose effect is to uniform a surface eliminating spikes and ripples due to noise and to image's blur, whereas the gradient effect is to find out and emphasize the edge of the image and it makes the External Energy responsible of an attraction action towards the object's edges [5], [6], [11], [13].

Solving the problem of finding the optimal object's contour means minimizing its related energy cost functional: by setting the first derivative of E_{snake} (with respect to s) equal to zero and solving the associated equation, the so-called Euler equations are obtained. Closed form solution of Euler equations cannot be computed in general, and numerical techniques, as the Gradient Descent Method, provide an unconstrained minimization procedure based on the use, as the search direction, of the opposite to the gradient. Thus, the iterative expression of the contour can be rewritten in terms of force's contributions that drive the snake towards the edge of interest, [6], [11], [13] both for the coordinate's vector $X(s)$ and $Y(s)$, as follows:

$$\begin{aligned} X^{k+1} &= X^k + \left(F^k_{x(elastic)} - F^k_{x(bending)} + F^k_{x(external)}\right)\Delta \\ Y^{k+1} &= Y^k + \left(F^k_{y(elastic)} - F^k_{y(bending)} + F^k_{y(external)}\right)\Delta \end{aligned} \tag{4}$$

where X^{k+1} and Y^{k+1} collect the coordinates of the update contour, and X^k and Y^k those of the current one; k is the iteration index, Δ is the algorithm step; parameters α, β and κ weigh the forces' contributions as for those of energies (see [20] for details).

2.2 Optimal Mass Transportation for Registrations and Processing of Biomedical Images

Optimal transportation issue was first formalized by G. Monge in 1781, rediscovered by Kantorovich in the context of economics and used in mathematics probability as a distance function (the Wasserstein metric). Formally, it concerns how to transport a mass (probability density) from one location (and distribution) to another, in such a way as to keep the transportation cost to a minimum. Indeed, the original problem concerned the minimization of transportation cost in moving a pile of soil from one site to another, thus, the Kantorovich-Wasserstein distance is also referred to as the earth mover's distance (EMD).

Optimal transport methods have appeared in econometrics, fluid dynamics, automatic control, transportation, statistical physics, shape optimization, expert systems, and meteorology. Moreover OMT problem has also been studied within context of imaging and computer vision applications [1], [24].

The Optimal Mass Tranportation problem: Monge and Kantorovich formulation We now give a formulation of the Monge-Kantorovich problem: in 1781 Monge formulated the problem in the Euclidean space; using a modern terminology, the measures replace the Monge mass densities for giving flexibility to the model [1], [10].

Given two mass distribution f^+ and f^- on $\mathbb{R}^N$, for which the principle of Mass Conservation holds:

$$\int_{\mathbb{R}^N} f^+(x)dx = \int_{\mathbb{R}^N} f^-(x)dx, \tag{5}$$

the Optimal Mass Transportation consists in finding, among all the maps carrying f^+ into f^- that with the minimum transportation cost, where the cost has a physical meaning and is proportional to the displacement. A such *tranport map t* is an element of the set

$$T(f^+,f^-) := \left\{t : \mathbb{R}^N \to \mathbb{R}^N \text{s.t. } t \text{ is measurable}\right\}, \tag{6}$$

that yields:

$$\int_{t^{-1}B} f^+(x)dx = \int_B f^-(x)dx, \forall \text{ Borel subset } B \text{ of } \mathbb{R}^N, \tag{7}$$

and minimizing the related cost:

$$min\left\{\int_{\mathbb{R}^N} |x-t(x)|\, f^+ d(x) : t \in T(f^+,f^-)\right\}. \tag{8}$$

The Kantorovich generalization of the Monge problem [1], [10], difficult to solve because of the non linearity of the problem itself, consist in switch from *transport maps* to *transport plans*, i.e. non-negative measures μ defined on $M\left(\mathbb{R}^N \times \mathbb{R}^N\right)$ and belonging to the set $P(f^+,f^-)$ that plays the same role of $T(f^+,f^-)$, satisfying the eligibility conditions:

$$\mu\left(B \times \mathbb{R}^N\right) = \mu^+(B) = \int_B f^+(x)dx$$
$$\mu\left(\mathbb{R}^N \times B\right) = \mu^-(B) = \int_B f^-(x)dx, \tag{9}$$

The cost transport minimization, by varying μ among the tranport plans, is defined as follows:

$$min\left\{\int_{\mathbb{R}^N\times\mathbb{R}^N} |x-t(x)|^p\, f^+ d(x) : t \in P(f^+,f^-)\right\}. \tag{10}$$

Kantorovich formulation shows some advantages: the linearity with respect to the structure of the vector space of $M(\mathbb{R}^N \times \mathbb{R}^N)$ and the new functional definition on a non-empty convex subset of M, $M(\mathbb{R}^N \times \mathbb{R}^N)$, where it is ensured the existence of the minimum, being lower semicontinuous for the topology. The new formulation contains the original one: in fact, if the map t is a transport, then the measure is defined by:

$$\mu_t(B) = \mu^+\left(\left\{x \in \mathbb{R}^N : (x,t(x) \in B)\right\}\right) \tag{11}$$

that is a transport plan and, moreover, the following relationship holds:

$$\int_{\mathbb{R}^N} |x-t(x)|\, f^+ d(x) = \int_{\mathbb{R}^N} |x-y|\, d\mu_t. \tag{12}$$

OMT approaches The OMT methodology allows to assess the deformations affecting objects within images, relying upon the problem of optimization built on the Kantorovich-Wasserstein distance, taken as a likelihood measure. Since object's deformations must respect the constrain of Mass Conservation (MC), the OMT method finds a match between two mass densities, assumed as the object's area weighted in the 2D case or the object's volume weighed in the 3D case.

The OMT focus is the computing of transport map t: approaches are based either on linear programming [17] or on the Lagrangian mechanincs [3]. The common idea is to reduce the OMT to a linear programing problem by approximating mass density measures between pairs of images, μ_0 and μ_1, as sums of δ functions:

$$\mu_0 = \sum_{i=1}^{N} \delta(x-x_i), \quad \mu_1 = \sum_{i=1}^{N} \delta(y-y_i). \tag{13}$$

Thus, for $2N$ point $(x_1,\ldots,x_N,y_1,\ldots,y_N) \in R^2$ the Kantorovich-Wasserstein metric is:

$$d^2(\mu_0,\mu_1) = min_\rho \sum_{i,j=1}^{N} \|x_i - y_j\|^2 \rho_{ij}. \tag{14}$$

Other approaches [7], [18], [22] quantify the deformation between pairs of images by exploiting the properties of the elastic materials. This method incorporated the Kantorovich-Wasserstein (or EMD) metric as a likelihood measure, that quantifies how close the images are, and the image transformation is calculated by minimizing it. The main advantages:

(1) Its parameters are free;
(2) It is symmetric;
(3) It does not require you to select reference points;
(4) The solution is unique;
(5) Takes into account density changes resulting from area or volume changes.

Briefly the OMT problem is recast as follows: let Ω_0 and Ω_1 be two subdomains of $\Re^d$ (for generality), with smooth boundaries, each with a positive density function, μ_0 and μ_1, respectively. We assume that the same total mass is associated with Ω_0 and Ω_1:

$$\int_{\Omega_0} \mu_0 = \int_{\Omega_1} \mu_1. \tag{15}$$

Considering a diffeomorphism $\tilde{u}$ from Ω_0 to Ω_1 which maps one density into the other one, and the MC assumptions, the relationship between two mass densities is expressed by:

$$\mu_0 = |D\tilde{u}|\mu_1 \circ \tilde{u}, \tag{16}$$

where $|D\tilde{u}|$ denotes the determinant of the Jacobian map $D\tilde{u}$, and $\tilde{u}$ the optimal mapping function [7], [22]. Accordingly with the MC principle, Eq. (16) implies that a small object in Ω_0, mapped into a large one in Ω_1 - or vice versa - must exhibit a corresponding decrease (increase) in density: a such mapping $\tilde{u}$ may be thought as a mass redistribution - of a material - from one distribution μ_0 to another μ_1. Hence, the issue is to find an optimal MC mapping, which minimizes the L^p Kantorovich-Wasserstein metric, rewritten as:

$$d_p^p(\mu_0,\mu_1) := \inf_{\tilde{u}\varepsilon MC} \int \|\tilde{u}(x) - x\|^p \mu_0(x)dx. \tag{17}$$

by computing the *cheapest* way to transport the mass from one domain to the other. Moreover, the optimal MC mapping thus defined is symmetric: the optimal mapping from Ω_0 to Ω_1 is the inverse of the optimal mapping from Ω_1 to Ω_0.

Different values of p parameter yield different optimal transport maps:

- for $p > 1$, the existence and uniqueness of the optimal transport map can be proved;
- for $p = 1$, the existence but not the uniqess of the optimal transport map can be proved;
- for $0 < p < 1$, the existence of a solution is not ensured.

The case $p = 2$ has been extensively studied and is that applied in this work for image registration and morphing.

3. DEFORMABLE MODEL AND OPTIMAL MASS TRANSPORTATION FOR TRACKING MOTION OF DCE IMAGES SERIES: RESULTS

Post-contrastographic Dynamic Constrast Enhancement (DCE) is a novel, yet consolidated, non invasive analysis procedure in the field of Biomedical Imaging for the assessment of the malignancy of lesions. Starting from the knowledge of the time evolution of the backscattered signal intensity corresponding to each Region Of Interest (ROI) - both organs or lesions - under investigation, a set of parameters useful for diagnosis are identified. Specifically, considering different images belonging to a series, it is possible defining the Contrast Enhancement (CE) curve (Fig. 1) as follows:

$$I(T_n, x, y) = [i(T_n, x, y) - i_0(x, y)], \tag{18}$$

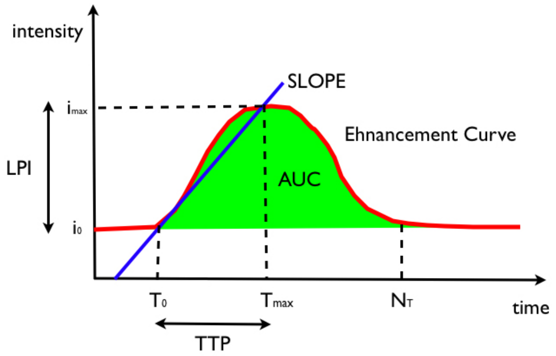

Figure 1. Contrast Enhancement Curve and related parameters.

where $i(T_n, x, y)$ is the image intensity value at the abscissa (x, y) at the sample time T_n and $i_0(x, y)$ is the basal value, i.e. the mean value of the intensity registered before the perfusion of the CA and assumed as background noise. Hence the CE curve represents the intensity change, of the backscattered signal, accordingly of the perfusion of the CA inside each single ROI. A set of parameters, AUC (Area Under Curve), LPI (Local Peak Intensity), TTP (Time To Peak) and SLOPE (Average Rising), useful for the diagnosis (Fig. 1), can be provied, in a compact fashion, by colour maps [12], [19].

The DCE analysis's crucial issue concerns with the goodness of the ROI approximation. A rough approach is to circumscribe the ROI with a polygon, project it along all the images belonging to the series and perform the DCE analysis on this coarse shape: that means including even tissues' portions out of the ROI (for the rough contouring procedure and for ROI movements). We have bettered the DCE analysis making it more accurate by improving the ROI's contour depiction, by means of AC, and assuming the hypothesis of rigid body motion: AC captures ROI's deformations and determines its best outline. In a previuos work [20] we implemented this approach by the Kernel Tracking (KT) of a fixed object - ROI's shape detected on the first frame - along the image series: a first analysis calculates - frame by frame - the coordinates of the center of mass and the principal axes of inertia of the ROI, then its movements are compensated by applying, to each pixel, rototranslation's displacements of the centre of mass. Even though this solution provided satisfactory results, rigid body motion assumption is still reductive, since it does not take into account ROI shape's deformations related, for instance, to breathing shifts, interior peristalsis and patient movements.

The Control Tracking Motion (CTM) strategy, here proposed, considers ROI's whole movement - displacements and deformations - following the OMT approach of the [18], in the case of $p = 2$, described in section 2.2.2. For each frame, we suppose that image's features provides information both for the object contouring and for mass density approximation; moreover we have performed several tests on images pairs by comparing the differences in the construction of the *optimal transport map t* between the case in which images present deformation with respect to the case in which they do not deform. The *optimal transport map t* is represented via a 3D matrix $t(i, j, k)$ and organized as follows: let n and m the row and coloumn dimensions of the initial images, then $i = \frac{n}{2}$ and $j = \frac{m}{2}$ are the row and column dimensions of the *transport map t* (dimensions are halved because pixels' pairs are analysed jointly), $k = 2$ because $t(:, :, 1)$ collects deformations along the first dimension, similarly $t(:, :, 2)$ collects deformation along the second dimension.

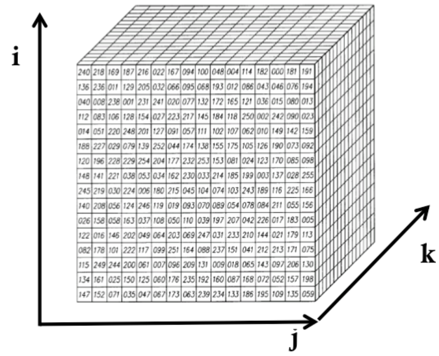

Figure 2. Transport Map sketch.

The line of attack of our procedure faced two main issue: first adapting the OMT code to process and analyse DICOM images, second performing the corrective actions for the DCE analysis. DICOM is the reference standard for Biomedical Imaging [16] and DICOM images are indeed metafiles which include graphics file (the image) and text data (patient information, exam's date, scanning mode, etc) used to handle the images themselves. The second issue presents two main steps: the analysis and the correction. The analysis step was aimed at collecting the required information on ROI deformations frame-by-frame, with respect to the first one, chosen as reference. We realized two main algorithms devoted to the deformations quantification on the basis of the *transport map*. Focusing on the first dimension of $t(i, j, k)$ we analyses the colums: as along them elements showed unitary hops it means images do not present deformations, otherwise as hops were bigger than 1 we could quantifiy the deformation (both as an expansion or a contraction) by evaluating the hop entity. The same procedure was applied focusing on the second dimension of $t(i, j, k)$ and analysing the rows. Once quantified - pixel by pixel - the deformations, we applied these results in the subsequent corrective action. It has been applied to each pixel belonging to the ROI shape frame-by-frame: for each of them, the corrective action provides a new ROI area (expanded or contracted), accordingly to the deformation analysis information, on which the subsequent DCE analysis will be performed.

We applied the OMT approach to improve the standard post-contrastographic Dynamic Contrast Enhancement (DCE) analysis of temporal series coming from the DCE-MRI images. Results are provided in terms of CE curve, aggregated color map (the AUC) and execution times comparison.

We carried out trials of the procedures on different body regions (Bowel Walls, Liver, Kidneys) affect by pathologies related to inflammatory disease or neoplasms. The acronyms in figure labels (3, 5, 7) refer to different cases as follows:

- **simple DCE**: post-contrastographic DCE analysis performed on a circumscribed polygonal ROI to the object and without any corrective action;
- **simple DCE + OMT**: post-contrastographic DCE analysis performed on a circumscribed polygonal ROI to the object and with OMT-based correction;
- **DCE + AC + KT**: post-contrastographic DCE analysis performed on a ROI detected by means of AC and with KT-based correction;
- **DCE + AC + OMT**: post-contrastographic DCE analysis performed on a ROI detected by means of AC and with OMT-based correction.

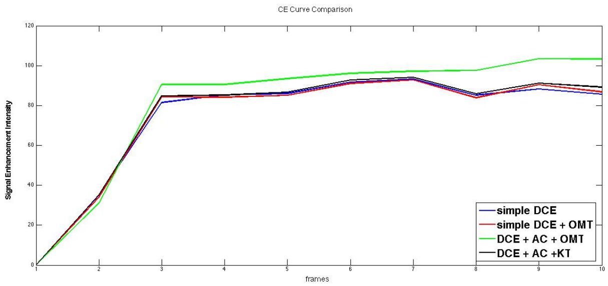

Figure 3. Dynamic Contrast Enhancement Curve comparison for Liver.

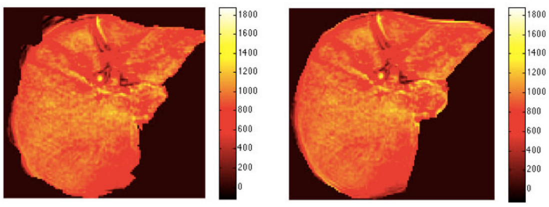

Figure 4. AUC map comparison: with (left) and without (right) OMT correction of Liver; high value refers to hypervascularized area within the parenchima.

Large organs as liver, for which the deformation can be negligible, may only admit the assumption of small displacements and therefore the use of a fixed -polygonal- outline for ROI detection provides a quite accurate estimate of the ROI intensity assessment over time (Figs. 3, 4); furthermore, an advantage of this approach is that the computational costs are drastically reduced because this analysis does not include the optimal transport map computing and the ROI correction (Fig. 9).

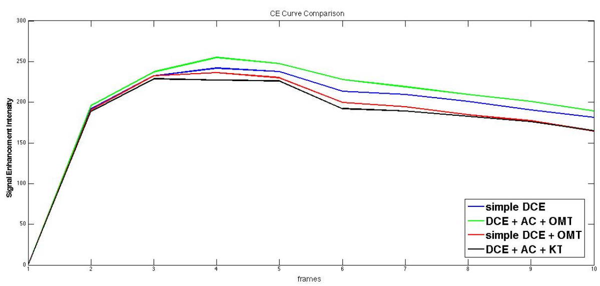

Figure 5. Dynamic Contrast Enhancement Curve comparison for Bowel Wall.

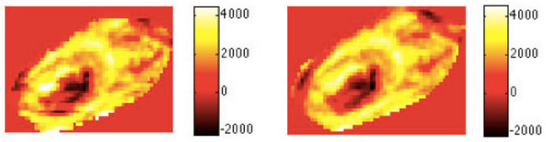

Figure 6. AUC map comparison: with (left) and without (right) OMT correction of Bowel Wall; high value refers to hypervascularized area within the parenchima.

Deformations and displacement affected more small organs and/or regions: thus improved apporaches can provide a more precise estimate of the ROI intensity trend over time (Figs. 5, 6, 7, 8); on the other hand, this techniques required a major cost timing (Fig. 9), because of the optimal transport map computing and the consequent corrective action of the ROI along the image series.

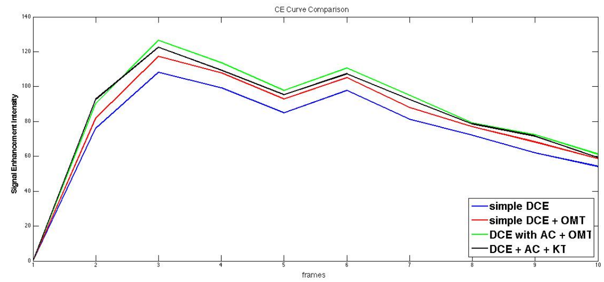

Figure 7. Dynamic Contrast Enhancement Curve comparison for Kidney.

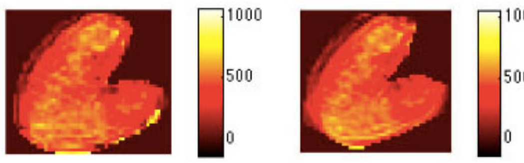

Figure 8. AUC map comparison: with (left) and without (right) OMT correction of Kydney; high value refers to hypervascularized area within the parenchima.

Figure 9 shows the difference in timing of the various approaches, whose goodness depends upon the required performances: greater the emphasis on speed of execution more it will prefer DCE analysis without corrective actions, greater the enphasis on tracking more it will prefer the improved procedure with AC and OMT.

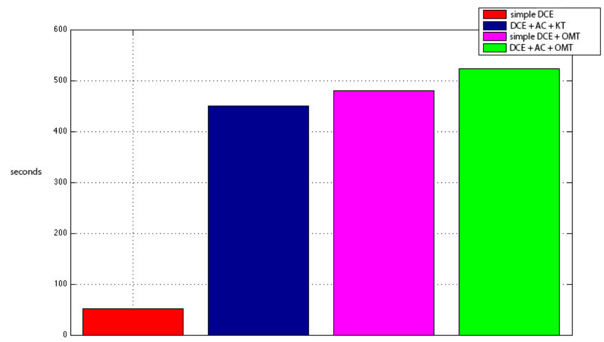

Figure 9. Tracking techniques: timing comparison.

4. DISCUSSION

We found that it is possible to improve the goodness of DCE analysis by combining AC and OMT techniques. The results showed that the corrective action is more effective as smaller and irregular is the analyzed region; on the other hand the image processing becomes time consuming, as the corrective action complexity increases. However in a clinical context, where the need is to make the diagnosis procedure both fast and accurate as possible, a tool that helps clinicians in this process, is welcomed.

The outcomes show that the combined approach, applied to organs of different shapes affected by different pathologies, provides encouraging results: large organs, as liver, suffer mainly from displacement movements due to patient breathing, whereas kidneys is affected by the contour's collapse due to the irregular shape, bowel wall pools both these aspects and is also influenced by deformations due to peristalsis movements. Our work's aim has been to improving the automatically assessment of pathologies, by facing all these drawbacks simultaneously and providing clearer results (CE curve over time and colour maps) to support the diagnosis procedure.

The Active Contour is a consolidated methodology normally used in the framework of biomedical imaging, whereas Optimal Mass Transport methods are widely applied in the context of image morphing and warping. Our work has exploited the best of both techniques and provided an application in the clinical diagnosis. The post-contrastographic DCE technique, a well-consolidated diagnosis procedure aimed at enhancing suspicious regions, provides the natural playground for the proposed approach.

Other improvements in future may come both from new MRI or CT techniques, that are becoming faster in the execution and not requiring the patient breath hold, and in the natural evolution of the procedure in the 3D case. In this direction one may hypothesize that aggregated parameters, as AUC color map, will provide information on the whole lesions, and comparing AUC maps of same patients in different times will be possible to follow up of a therapy and avoid invasive (hystological) exams.

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