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Towards a Novel Approach for Tumor Volume Quantification

Amina Kharbach * , Benaissa Bellach, Mohammed Rahmoune, Mohammed Rahmoun and Hanane Hadj Kacem

LSE2I Laboratory, National School of Applied Sciences, Mohammed First University, 60000 Oujda, Morocco; b.bellach@ump.ac.ma (B.B); m.rahmoune@ump.ac.ma (M.R.); m.rahmoun@ump.ac.ma; (M.R.); h.hadjkacem@ump.ac.ma (H.H.K.)

* Correspondence: a.kharbach@ump.ac.ma; Tel.: +212-6659-19707

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Abstract: In medical image processing, evaluating the variations of lesion volume plays a major role in many medical applications. It helps radiologists to follow-up with patients and examine the effects of therapy. Several approaches have been proposed to meet with medical expectations. The present work comes within this context. We present a new approach based on the local dissimilarity volume (LDV) that is a 3D representation of the local dissimilarity map (LDM). This map presents a useful means to compare two images, offering a localization of information. We proved the effectiveness of this method (LDV) compared to medical techniques used by radiologists. The result of simulations shows that we can quantify lesion volume by using the LDV method, which is an efficient way to calculate and localize the volume variation of anomalies. It allowed a time savings with the compete satisfaction of an expert during the medical treatment.

Keywords: lesion; therapy; local dissimilarity volume; local dissimilarity map

1. Introduction

Recently , medical practice has known veritable revolution, thanks to new imaging techniques [1–3]. Diagnosis became more accurate and quality of care is now better. Methods found in the literature for volume comparison can be classified into two approaches:

(a) Global techniques based on volume comparison algorithms [4,5]: they are based on statistical properties in voxel-to-voxel comparison. Generally, the global methods synthesize the whole image information and do not pinpoint the local dissimilarity information.
(b) Local algorithms based on dissimilarity map [6–9] and strain field [10].

Although many methods have been proposed, the problem of precision in the definition of this volume always arises due to the movement of the body during the image acquisition. This work gives a novel approach to calculating lesion volume based on local dissimilarity volume. We applied it to volume measurement used by radiologists. Our objective is to help them in locating variations and calculating the volume of a tumor. Our study shows the efficiency of methods based on local measure by reducing the calculation time and localizing differences during medical treatment.

Our paper is organized into different sections. Section 2 presents the classical comparison methods of lesion volume and a list of software helping radiologists to perform calculations automatically. Section 3 summarizes methods based on local dissimilarity measures. Finally, the discussion of the experimental results and the conclusion are respectively reported in Sections 4 and 5.

2. Classical Estimation Methods

In clinical practice, the operative tumor volumes are often based on measuring the greatest axis of the tumor in x and y directions. In this section, we highlight different methods used by radiologists to evaluate volume growth:

- Volume ellipsoid formula ($3\pi/4 \times length \times depth \times width$) for tumor having spherical shapes; however, this method is less accurate because of the irregular form of the majority of tumors.
- The voxel counting approach; i.e., counting all voxels and multiplying the total by the voxel volume.
- Anti-aliasing voxel counting as defined in [4] can be done by incorporating the data obtained from each of the multiple slices. The anti-aliasing step reduces artifacts that result in visualization of binary surfaces.

Several companies share the equipment market dedicated to the study of medical images [11]. They propose complete offers of high technology products involved in all stages of the digital imaging chain (acquisition, image processing, image analysis, etc.) such as:

- Vitrea Advanced by Vital image [2], which segments the area of interest with one click, automatically calculates the density and diameter of each nodule, displays 3D views, and offers a comparative mode to establish the time elapsed and the increase percentage in volume using data from computed tomography (CT scan) or magnetic resonance imaging (MRI). Figure 1 shows an example of measurement realized by Vitréa Advanced.
- Analyze has been designed and developed at the Mayo Clinic's Biomedical Imaging Resource (BIR) [3]. It gives tools for the display and analysis of multidimensional biomedical images.
- ATOMImage developed by Xortec® is software that makes it possible to treat volumetry automatically. It is easy to use and it offers a very remarkable time savings by guaranteeing a great reproducibility compared to the manual methods. It is a fast practical tool for Stroke cases. It is applicable for oncology in order to have an organic assessment and to follow the tumor's growth. It can segment the image treated in one click and display 3D views. Moreover, ATOMImage can automatically calculate diameters and densities in order to have true volumes and not a geometrical approximation. It also establishes time runs out, the doubling time, and the percentage increase in volume.

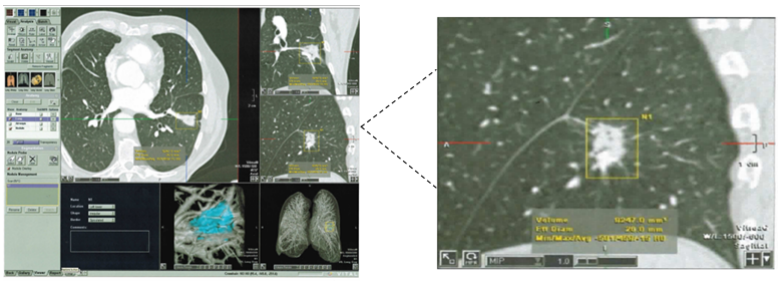

Figure 1. Calculation volume example on magnetic resonance imaging (MRI) medical image by Vitréa Advanced.

All calculation methods call for segmentation (manual/automatic), which represents an important process in image analysis. It is the heart of any system of vision which aims at extracting visual volumes over time. Multiple papers have been proposed to improve and accelerate it [12–14]. Volume measurements give absolute values and do not take into account the localization of anomalies in images. In this case, we will describe two methods realizing this criterion in the next section .

3. Local Measures

3.1. Strain Field

Classical techniques for monitoring tumors in 3D consist of their contouring in the scanned images of the patient at two different instants. The variation between the two volumes extracted is then an indication of the desired delta. However, this approach can be difficult for at least two reasons:

- The need for contouring (manual or assisted)
- Segmentation errors

A more advanced approach involves the establishment of a non-rigid registration between the two internal body parts, thereby defining a strain field between the two acquisition instants. The non-rigid registration seems to be necessary because of the morphological changes due to breathing or changes in patient position between two acquisitions. Most medical imaging bases the detection of tumors on the extraction and analysis of characteristics (intensity, texture, shape, etc.), but these techniques give absolute value and do not take into account the dynamic information in the image. Strain field analysis allows the detection of active lesions, and gives the quantitative measurement of variation volume. This method has been successfully tested on the brain [10]. We have classified this method as local because it is based on a vector field presenting a lesion's deformation over time. The advantage of this technique is its ability to visualize invisible lesions that have the same intensity as unharmed tissue.

In order to quantify volume, the author used the Green–Ostrogradsky theorem (1) by integrating the progression or regression field on nested surfaces marrying the shape of the evolutionary structure.

$$div \int_V div(f)dV = \int_{\partial V} f.ndS \tag{1}$$

where f is the strain field, V is the closed volume, and n is the outward normal vector.

The author of [10] supposed a volume V included in a closed surface S, and a regular grid G that recovers V. The lesion volume is the number of nodes of G contained in V multiplied by the volume of one voxel. V volume tends towards the exact value when the step of G tends towards 0.

3.2. Local Dissimilarity Volume

The local dissimilarity volume (LDV) derives a local measure of dissimilarity for 3D binary images by comparing images locally with a sliding volume, where Hausdorff distance is the chosen measure to determine the degree of dissimilarity between two objects [15]. LDV is defined as:

Given two non-empty finite sets A and B of points of R^3, the local dissimilarity volume is defined as follows:

$$\forall x \epsilon \mathbb{R}^3, LDV = \begin{cases} HD_{B(x,r_{max})}(A,B) & if \quad R \neq \emptyset \\ 0 & if \quad R = \emptyset \end{cases} \tag{2}$$

where R represents the local measure set and it presents the measure of the local Hausdorff distance in the window $B(x,r)$ of center x and radius r. It is given by:

$$R = \left\{ r > 0 / HD_{B(x,r)}(A,B) = r \right\} \tag{3}$$

The general expression of HD with an underlying distance d is given by:

$$HD(A,B) = max\left(hd(A,B), hd(B,A)\right) \tag{4}$$

with direct Hausdorff distance is expressed as follows:

$$hd(A,B) = max_{a \epsilon A}(min_{b \epsilon B} d(A,B)) \tag{5}$$

respectively

$$hd(B,A) = max_{b\epsilon B}(min_{a\epsilon A}d(B,A)) \quad (6)$$

The Algorithm 1 below illustrates the stopping criterion given in Equation (3)

Algorithm 1: Computation of stopping criterion.

For each fixed voxel x **do**
n:=1
While $HD_{B(x,n)}(A,B) = val_{max}$
n:= n+1
End While
Return $HD_{loc} = HD_{B(x,n-1)}(A,B)$
End

This method has been successfully applied on segmented MRI tumor volumes by localizing true tumor growth [6].

Let us consider two volumes $m \times m \times m$. The local dissimilarity volume calculation is a loop that is carried out to calculate the local dissimilarity measure in each point:

- For each voxel, the size of the window W is incremented from the initial size until the final size is reached $r_{max} \times r_{max} \times r_{max}$ with $r_{max} < m$.
- Calculation is carried out for the $m \times m \times m$ voxels.

For each voxel, there are $O(m^3)$ operations. The algorithmic complexity of the local dissimilarity voxel is thus $O(m^6)$.

For this reason, we restricted our study by using the distance transform (**td**) that makes it possible to know the distance between a given voxel and the nearest one [16,17]. It allows fast calculations and ensures $O(m^3)$ for the algorithmic complexity. The reduced expression based on transform distance is given by:

$$LDV = |Vol2 - Vol1| \times max\,(td(Vol1), td(Vol2)) \quad (7)$$

In our case, we used a weighted distance transform algorithm because of its simplest implementation and its fastest execution time.

4. Proposed Approach

The tumor volume calculation with precision is primordial in order to plan the continuation of the treatment. The World Health Organization (WHO) defined standardized criteria of volume evaluation that are based on the product of the largest diameter of the tumor and the perpendicular largest one, as well as the described methods in Section 2. The practitioner thus carries out these operations with each volume in order to define the tumoral measured answer. However, those criteria do not define the localization nor the quantity of lesions to be measured in the case of multiple tumors. To mitigate this disadvantage, we proposed a method based on the direct application of the volume calculation methods on the exact difference detected by the local dissimilarity volume, as shown in Figure 2.

If the tumor presents a regression of at least 50% , the tumoral answer is incomplete (partial answer PR); between a regression of 50% and a progression of 25%, the tumor is stable (stable disease SD); and when the progression exceeds 25% we have a tumoral progression (progressive disease PD).

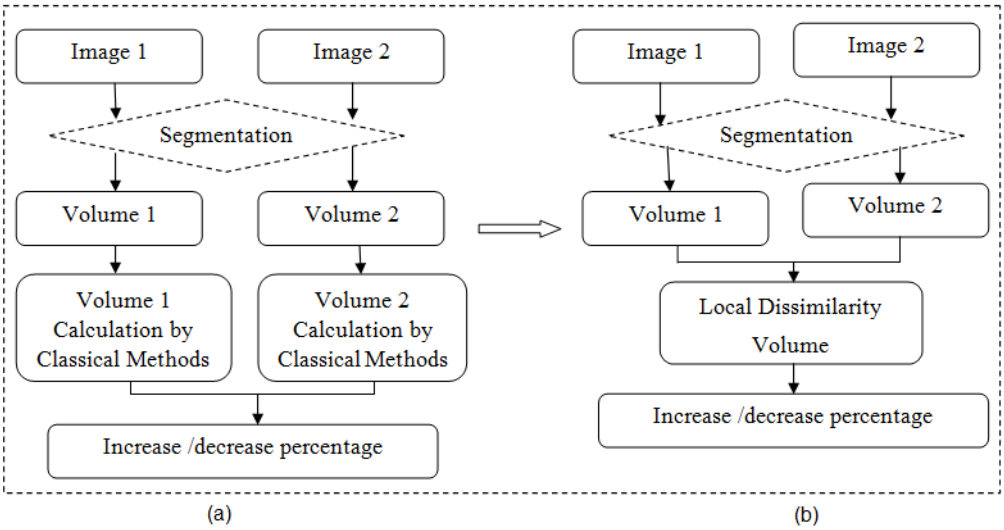

Figure 2. Novel approach of volume calculation using the local dissimilarity volume. (**a**) Classical approach for volume calculation; (**b**) Proposed method.

5. Experimental Results

The objective of this work is to propose a novel approach for volume evaluating. We worked as a first step on the MRI and X-ray medical images procured from clinical imaging for patients with different types of anomalies. In this study, we first implemented the local dissimilarity volume based on gray-weighted distance transform [18] in segmented MRI medical images of a patient suffering from mediastinal lymphoma for three months. We do this in order to visualize the difference and to then apply some of the methods quoted above for volume calculation. The proposed approach requires a preliminary segmentation of the treated zone. To ensure this step, we used the ITK-Snap software, wjocj provides semi-automatic segmentation using active contour methods [19]. The example in Figure 3 shows the result of the implementation of the local dissimilarity volume in one slice of a medical image.

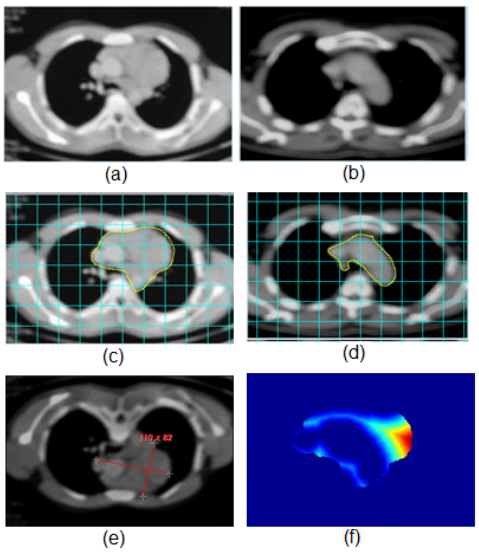

Figure 3. Novel approach to volume calculation using the local dissimilarity volume. Two MRI medical images: (**a**–**d**) MRI Images after segmentation; (**e**) Classical approach for volume calculation; (**f**) Local dissimilarity map between (**c**,**d**).

Generally, the image registration is an invaluable step to align medical images. For that, we can use the normalised dissimilarity index described in our former work [20,21]. In this paper we proved that our proposed method is a good tool to register both binary and grayscale images.

To evaluate the volume measurement, we applied voxel counting and, anti-aliased voxel counting measures on the local dissimilarity volume in order to compare results with those obtained by radiologists using either the ellipsoid formula or Vitréa Advanced.

Any voxel was assumed to be of dimension 1 mm $\times$1 mm $\times$1 mm, and the results are shown in Tables 1–3. We note that besides asserting anomalies between two acquisitions (Figure 3), the local dissimilarity volume allows us to directly point out volume variations, and this goes without using the classical methods adopted by radiologists that separately calculate each volume before estimating the variation. We then calculate the computation time of these methods for each patient, and note that the total time of the measurement used by radiologists for only one patient was 12 min, while the other based on the local dissimilarity volume was 5 min 35 s. So, we can deduce that we can reduce computation time by directly implementing volume measurement methods in the local dissimilarity volume.

Table 1. Voxel counting applied on the local dissimilarity volume (LDV). VCM: volume calculation method.

VCM/Patients	Voxel Counting			
Volume (mm^3)	Vol 1	Vol 2	Difference	LDV
Patient 1	34,510	25,139	27%	27%
Patient 2	2687	3754	39%	39.8%
Patient 3	90,450	81,993	9.34%	9.31%
Patient 4	6522	5766	11.6%	11.68%

Table 2. Anti-aliasing voxel counting applied on the local dissimilarity volume.

VCM/Patients	Anti-Aliasing Voxel Counting			
Volume (mm^3)	Vol 1	Vol 2	LDV	Difference
Patient 1	34,627	25,224	27.1%	27.16%
Patient 2	2695	3764	39.6%	39.95%
Patient 3	90,785	82,272	9.34%	9.35%
Patient 4	6543	5785	11.58%	11.71%

Table 3. Volume difference percentage obtained by classical method used by radiologist and Vitrea Advanced software.

V.Diff	Radiologist	Vitrea Advanced
Patient 1	27.15%	28.19%
Patient 2	39.65%	40.52%
Patient 3	9.35%	10.17%
Patient 4	11.58%	12.49%

As seen in the tables, volume calculation methods (VCMs) applied on the local dissimilarity volume provide accurate results compared to the volume difference percentage. The voxel counting measure is closer than 0.42 to the true value, while the anti-aliased measure is closer than 0.078 to the true one.

6. Conclusions

Medical images are without doubt incredibly rich information. Clinicians can evaluate the appropriateness of a treatment by comparing changes in the volume of treated lesions. In this paper,

we can show the efficiency of local dissimilarity volume to localize and quantify tumor development changes. This approach is a remarkable time-saver for radiologists and provides a potentially useful assessment of tumor growth or cure. For our next work we will try to optimize these algorithms in order to track tumors over time.

Author Contributions: Amina Kharbach participated in all experiments, coordinated the data-analysis and contributed to the writing of the manuscript. Benaissa Bellach participated in the experiments, coordinated the data-analysis. Mohammed Rahmoune participated in the experiments and coordinated the data-analysis. Mohammed Rahmoun designed the research plan and organized the study. Hanane Hadj Kacem is the radiologist; she validated the obtained results and compared them with classical methods.

Conflicts of Interest: The authors declare no conflict of interest.

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