

On the Intensity-Curvature Functional of the Bivariate Linear Function: The Third Dimension of Magnetic Resonance 2D Images in a Tumor Case Study

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Abstract The Intensity-Curvature Functional is a mathematical engineering instrument which is calculated using the following procedure. The ratio between: (i) the product between the signal-image pixel intensity and the Classic-Curvature, both of them calculated at the grid node of the sequel of digital samples; and (ii) the product between the signal-image and the Classic-Curvature, both of them calculated at the intra-pixel location chosen for re-sampling the sequel of digital samples. This manuscript reports on the following phenomenon observed when using the bivariate linear function to model the signal-image data and to calculate the Intensity-Curvature Functional of 2D Magnetic Resonance Imaging (MRI) of a human brain affected by a tumor. A third dimension perpendicular to the image plane appears from the two-dimensional MRI images. The third dimension highlights the features of the 2D image and allows the identification of the tumor contour line.

Keywords Classic-Curvature, Contour Line, Intensity-Curvature Functional, Re-sampling, Third Dimension

1. Introduction

The identification of the tumor margins (or contour line enclosing the tumor) both during pre-surgical and surgical resection is very important and has been studied using nanoparticle metabolism [1]. The aforementioned identification of the contour line of the tumor in MRI is a task which is achieved as a consequence of the segmentation of the tumor from MRI. In order to segment the human brain tumor volume from MRI a study reports on a signal processing technique based on supervised k-nearest neighbour (kNN) rule and fuzzy methods [2]. The aforementioned study mentions that the results of the signal processing technique are patient-dependent. To determine human brain tumor MRI segmentation the literature also reports on high accuracy statistical methods [3, 4]. Also, the literature reports on a technique called "Fluid Vector Flow" (FVF) active contour model [5] which was claimed to be superior to: gradient vector flow techniques [6]; boundary vector flow techniques [7]; and magnetostatic active contour techniques [8]. Another signal processing technique to segment and classify the human brain tumor from MRI

uses a brain atlas and a patient dependent abnormal tissue prior obtained from Magnetic Resonance Spectroscopic Imaging [9]. Within the context of MRI tumor segmentation, another important task is the measurement of the tumor volume and such task has been accomplished in literature through techniques which employ MRI signal processing based on fuzzy c-means and a non-fuzzy clustering algorithm [10], and also through an approach based on the Adaptive Template moderated Classification [11], which was later developed further into an automatic segmentation method of brain tumors imaged with MRI [12]. Also, in order to measure the volume of the tumor, methods based on manual trace and on threshold are reported in literature [13].

1.1. The Rationale

The rationale of the works herein presented is that one of extracting the third dimension from 2D MRI images. The third dimension is perpendicular to the images. The method employed to undertake the extraction of the third dimension is the Intensity-Curvature Functional of the bivariate linear formula and such method has been successful as the results section shows.

1.2. The Intensity-Curvature Functional

Recent research has presented the calculation of the Classic-Curvature from 2D and 3D images [14]. The

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Classic-Curvature is calculated on a signal-image through the summation of all of the second order derivatives of the Hessian of the model function fitted to the image data. It has been clarified elsewhere [14] that the requirement for the calculation of the Classic-Curvature is that one of the second order differentiability of the model function. In the present works the model function which is fitted to the Magnetic Resonance Imaging data is the bivariate linear interpolation formula [15, 16]. The Classic-Curvature is the signal processing engineering solution which provides with the formulation of the Intensity-Curvature Functional (ICF) [15, 16]. The formula of the Intensity-Curvature Functional, when the model function fitted to the signal-image data is the bivariate linear, has been reported elsewhere [15-17]. Re-sampling the discrete sequel of digital samples is inherent to the calculation of the ICF. Specifically, since the ICF is the ratio between two terms, the term at the numerator (called intensity-curvature term before interpolation) is computed at the grid node of the discrete sequel of pixels intensity, whereas the denominator (called intensity-curvature term after interpolation) [15-17] is computed at the intra-pixel location where the signal-image data is re-sampled through the model function. The next section of the manuscript reports the compact form of the basic formulae for the calculation of the Intensity-Curvature Functional when the model function is the bivariate linear function. The results section shows the third dimension obtainable through the calculation of the ICF on the basis of the tumor MRI. The discussion section addresses the placement of the present works within the context of the current literature, and also the major finding, which is that one of the extraction of the tumor contour line through the visualization of the third dimension of the 2D MRI. The finding that the third dimension is capable to highlight human brain features observable in 2D MRI, and most importantly, the finding that the third dimension allows the identification of the tumor contour line, is subsequent to the use of the Intensity-Curvature Functional. The aforementioned identification of the contour line enclosing the tumor is the discovery of the studies herein reported and such discovery is consequential to the rationale.

2. Theory

Let $h(x, y)$ be the bivariate linear interpolation function as per equation:

$$h(x, y) = f(0, 0) + x \theta_x + y \theta_y + xy \omega_f \quad (1)$$

$$\theta_x = f(1, 0) - f(0, 0) \quad (2)$$

$$\theta_y = f(0, 1) - f(0, 0) \quad (3)$$

$$\omega_f = f(1, 1) + f(0, 0) - f(0, 1) - f(1, 0) \quad (4)$$

Where $f(1, 0)$, $f(0, 1)$ and $f(1, 1)$ are the values of pixel intensity at the three edges of the pixel which intensity

value is $f(0, 0)$. The Classic-Curvature of the bivariate linear function (1) is given in equation (5) and it is the sum of all of the second order derivatives of the polynomial with respect to all of the variables and all the covariates.

$$\Theta(x, y) = \left(\frac{\partial^2 h(x, y)}{\partial x^2} \right) + \left(\frac{\partial^2 h(x, y)}{\partial x \partial y} \right) + \left(\frac{\partial^2 h(x, y)}{\partial y \partial x} \right) + \left(\frac{\partial^2 h(x, y)}{\partial y^2} \right) \quad (5)$$

Let the intensity-curvature term before interpolation $E_0(x, y)$ [17], and the intensity-curvature term after interpolation $E_{IN}(x, y)$ [17] be defined as per equation (6) and (7).

$$E_0 = E_0(x, y) = \int_0^x \int_0^y h(0, 0) \cdot \Theta(x, y)_{(0, 0)} dx dy \quad (6)$$

$$E_{IN} = E_{IN}(x, y) = \int_0^x \int_0^y h(x, y) \cdot \Theta(x, y)_{(x, y)} dx dy \quad (7)$$

The definition of the Intensity-Curvature Functional is:

$$\Delta E(x, y) = \frac{E_0(x, y)}{E_{IN}(x, y)} \quad (8)$$

3. Results

The results presented in this section were obtained through the calculation of the Intensity-Curvature Functional when fitting to MRI images the bivariate linear function. The key point of this work is to demonstrate that through the use of the ICF of the bivariate linear function, it is possible to extract the third dimension from 2D MRI images and to identify the contour line of the tumor. The third dimension is perpendicular to the image plane. As the results show, along with the third dimension, it is generally possible to highlight the features of the MRI, and in the specifics, the relevant features of the tumor such as the contour line. The misplacement used to re-sample the MRI images when calculating the ICF was $(x, y) = (0.5\text{mm}, 0.5\text{mm})$ in all of the cases presented in this manuscript.

Figure 1 shows the original MRI in (a) and the ICF in (b). The third dimension is discernible in (b) and the highlight of the features has two main characteristics. The two characteristics are shown in (a) and they are: the bright and the dark nuances, both of them presumably fluids of the tumor. It is visible that the dark regions of the tumor in (a) are shown in valleys in (b), whereas the bright regions of the tumor in (a) are shown in mounts. The valleys are at the level of the image plane, whereas the mounts are on a higher elevation along the third dimension perpendicular to the image plane which is perceptible when looking at the ICF image in (b). Another characteristic of the ICF shown in (b)

is that the entire region of higher elevation is surrounded by the tumor contour line.

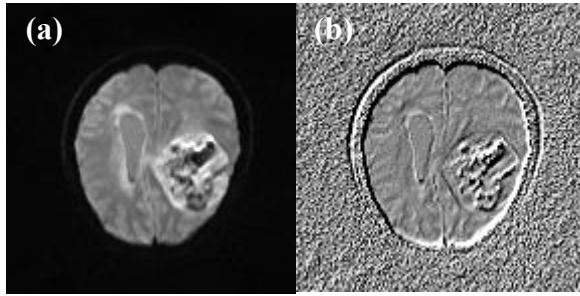


Figure 1. In (a) is shown the original MRI with pixels matrix size of 160×160 and pixel size of $1.0\text{mm} \times 1.0\text{mm}$. In (b) is shown the ICF of (a). Consequently, also the ICF is a 160×160 pixels image. The ICF shows a third dimension made of valleys corresponding to the dark nuances seen in (a), and mounts corresponding to the bright nuances seen in (a). The region of higher elevation in (b) shows the tumor contour line

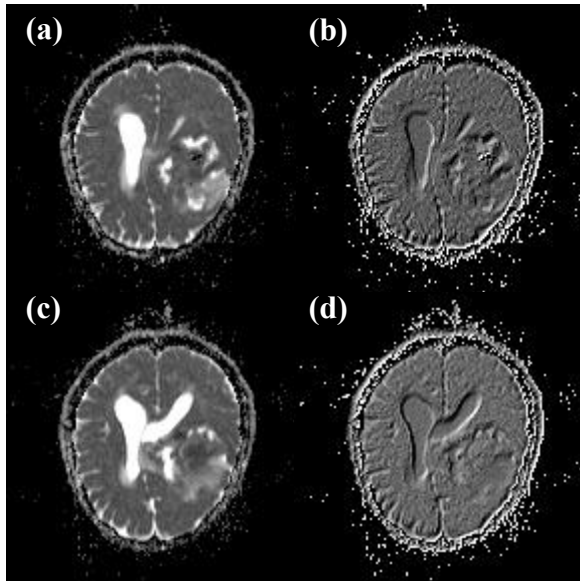


Figure 2. The original MRI is shown in (a) and in (c) and the corresponding ICFs are shown in (b) and in (d). The pixels matrix size is 160×160 and the pixel size is $1.0\text{mm} \times 1.0\text{mm}$ in both of (a) and (c). Consequently, also the ICF is a 160×160 pixels image. The emphasis in this figure is in the third dimension shown by the Cerebrospinal Fluid (see (b) and (d)) and the white nuances of the tumor which also show the third dimension in (b) and in (d). The contour line of the tumor appears scattered in both (b) and (d)

Furthermore, it is visible in (b) the elevation of the borderline of the ventricle. The ventricle appears flat in (a) whereas it has a third dimension in the ICF shown in (b). Figure 2 highlights the ventricles, the Cerebrospinal Fluid (CSF), and the tumor region as shown in (a) and in (c). The CSF is given the third dimension in (b) and in (d) where the ICF is shown. Consequently, also the ventricles of the human brain are highlighted in (b) and in (d). Additionally, the white nuances of the tumor shown in the original MRI in (a) are those which are elevated from the image plane in the ICF shown in (b) and in (d). Apart from the regions of the tumor which show no white nuances, the tumor region seen in (a) and in (c) remains flat in (b) and in (d). Figure 2 thus

suggests that the ICF is more likely to extract the third dimension along the axis perpendicular to the image plane, for those regions which show the nuances of the tumor. This was already seen in Figure 1 where the third dimension is distinguishable for both white and dark nuances (see Figure 1b). The contour line of the tumor seen in Figure 2b and Figure 2d is not clearly discernible as the one seen in Figure 1b.

Figure 3 is an example of how the third dimension visible in the ICF extends to the entire region of the tumor. In the MRI shown in (a) the tumor shows a white nuance across the entire pathological region. Also, the tumor shows a considerable pressure on the ventricle. The aforementioned observations are corroborated through the ICF shown in (b). Specifically, the entire white region seen in (a) has its third dimension shown in (b) of Figure 3. Also, the borderlines of the ventricles have a third dimension in (b) whereas the CSF is depicted as noise because is imaged in black in (a). This case of the CSF seen in Figure 3b is the opposite of what seen in Figure 2 where the CSF is imaged in white in the original MRI. In Figure 3 instead, the CSF is imaged in dark in the original MRI (see (a)) and so is shown as if it was noise in the ICF (see (b)). It is important to stress that in this case the ICF is not an accurate representation of the CSF. Moreover, the ICF seen in Figure 3 shows a remarkable capability to reproduce the sulci of the human brain which is perceivable through the third dimension which adds information relevant to the depth of the sulci. The contour line of the tumor is clearly seen in (b) because of the higher elevation of the tumor which is located above the image plane.

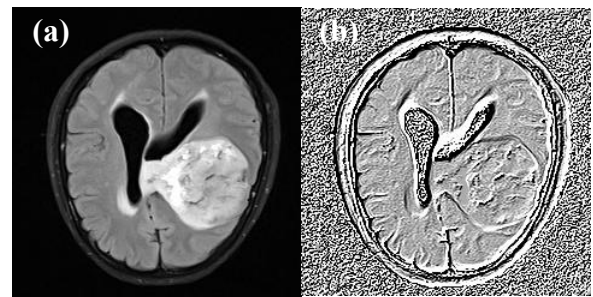


Figure 3. The original MRI is shown in (a) and the ICF is shown in (b). The pixels matrix size is 260×320 with pixel size of $1.00\text{mm} \times 1.00\text{mm}$. The images were cropped so to highlight the region of interest. The ICF has also matrix size of 260×320 pixels. This picture shows the tumor with a large and extended white nuance observable in (a) and the corresponding third dimension seen in (b) in the ICF. Also visible is the third dimension of the contour of the ventricles. The contour line of the tumor is clearly demarcated in (b)

Figure 4 shows in (a) the original MRI and in (b) the ICF. The ICF provides with the third dimension at the location of the tumor and the third dimension covers the tumor full spatial extent. The ventricle is elevated along with the anatomy of the skull and also the subcortical regions. The interesting feature of the ICF is that one of showing one level of elevation from the image plane in correspondence of the white nuances shown in (a), see white arrows in (a) and in (b). Additionally, in between the two arrows, the tumor region

shown in (a) shows some dark spots (presumably blood or other fluids), see black arrow in the ICF image shown in (b). The ICF image shows the third dimension corresponding to the dark spots (see black arrow in (b)). Also in figure 4 the contour line of the tumor is clearly shown and this fact is a consequence of the third dimension extracted through the ICF.

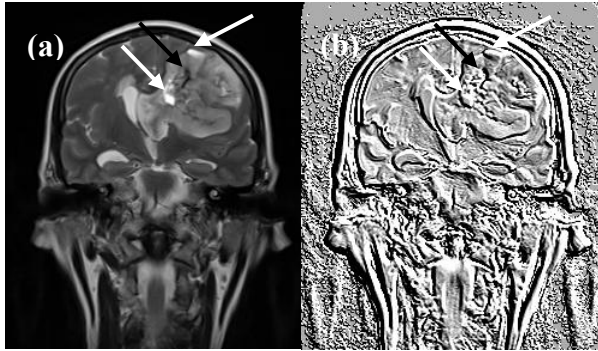


Figure 4. The original MRI is shown in (a) whereas the ICF is shown in (b). The pixels matrix size is 262×320 with pixel size of $0.78\text{mm} \times 0.78\text{mm}$ for both (a) and (b). The images were cropped so to show the region of interest. The ICF shows clear and distinguishable regions where the third dimension is visible, specifically in the tumor region, the ventricles, the anatomy of the skull and the subcortical regions. The contour line of the tumor is clearly shown and clearly distinguishable and is located on a plane which is more elevated than the image plane

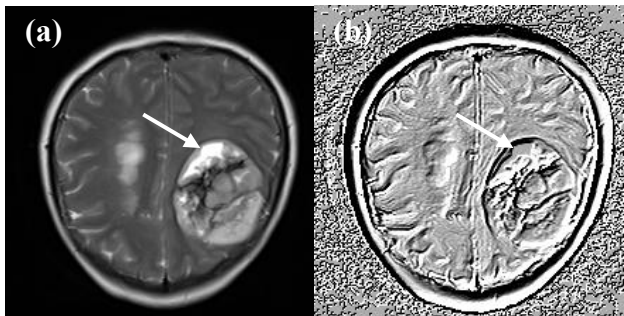


Figure 5. The original MRI is shown in (a) and the ICF is shown in (b). The pixels matrix size is 262×320 with pixel size of $1.0\text{mm} \times 1.0\text{mm}$ for both (a) and (b). The images were cropped so to highlight the regions of interest. The ICF shows the third dimension in the region of the tumor, also in the CSF of the right ventricle and in the proximity of the sulci of the human cortex. The contour line of the tumor is clearly demarcated throughout its full spatial extent

Figure 5 is particularly interesting because of the capability of the ICF to extract the third dimension for both white and dark nuances (which are shown in the region of the tumor in (a)). The tumor appears on a higher level of elevation when compared with the rest of the human cortex, and the sulci of the cortex are shown on a plane of elevation which is higher than the level of placement of the white matter of the brain. The contour line of the tumor is shown clearly all around the pathology and is divided in two separate parts. One part (see region of the contour line in proximity of the arrow in (b)) is located on a lower elevation and the remaining part is located on a higher elevation in relationship to the image plane. In (b), the ICF of the tumor is made of three main regions: one is white and corresponds to

the dark nuance of the tumor visible in (a); the other one is grey and corresponds to the tumor structures seen in grey in (a); and the last one is dark and corresponds to the 'u' shaped line which is inside the region of the tumor and is shown in dark in (a). The region in grey in (b) which is pointed by the white arrow appears to be on the third dimension when compared to the corresponding area seen in white in (a) (see white arrow in (a)).

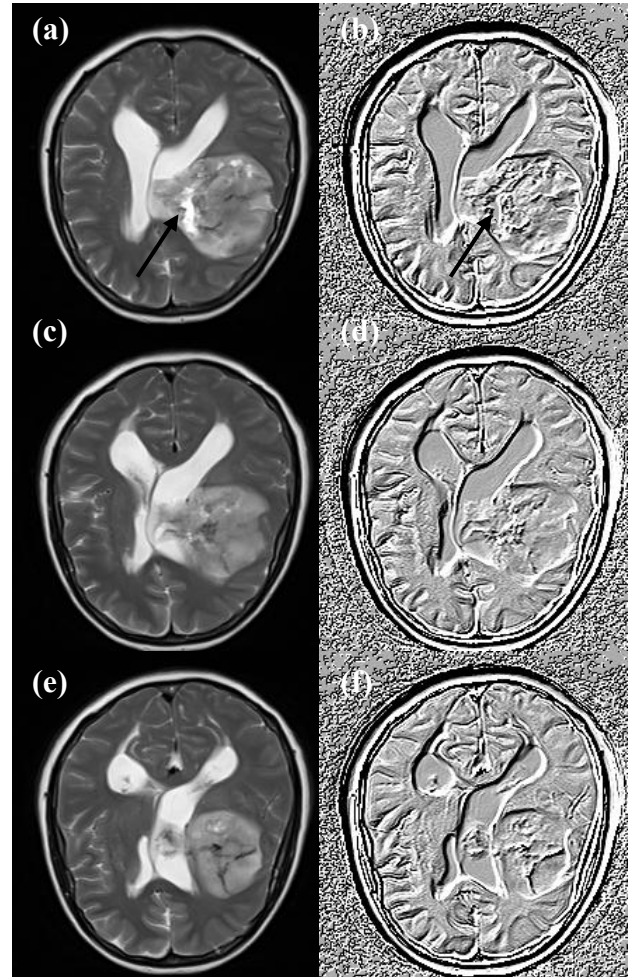


Figure 6. The original MRI is shown in (a), (c) and (e) and the corresponding ICF images are shown in (b), (d) and (f). The images comprise of a pixels matrix size of 262×320 with pixel size of $0.78\text{mm} \times 0.78\text{mm}$. The images were cropped so to show the regions of interest. The ICF shows the third dimension across the all human brain with specific focus on the tumor area, the ventricles and the CSF, and also the depth of the sulci. The dark arrow indicates the third dimension of the white nuance of the tumor shown in (a), (see (b)). The third dimension perpendicular to the image plane shows the contour line of the tumor clearly distinguishable in (b), (d) and in (f)

Figure 6 shows another example of the capability of the ICF to extract the third dimension from a two dimensional MRI. The third dimension is visible in (b), (d) and (f) for what pertains to the tumor in its entire spatial extent and with specific focus on the white nuance indicated by the dark arrow in (a), which is highlighted in (b). Also, the third dimension is visible in (b), (d) and (f) in the ventricles, the CSF and the sulci of the human brain cortex. In fact, when

looking at the ICF images in (b), (d) and (f), both of the ventricles (along with the CSF), and the tumor area in its full spatial extent, are placed on a plane of higher elevation when compared to the image plane shown in (a), (c) and (e). The contour line shows characteristics which are consistent with the relative position between the ventricles and the tumor mass. Specifically, in (b) and in (d) the contour line intersects the ventricles consistently with the pressure exercised by the tumor on the ventricles. Also, in (e) the tumor exercise pressure on the ventricle region, however with reduced spatial extent as it is visible that there is a mixture of CSF and tumor structures. Consistently with what seen in (e), the contour line in (f) is clearly demarcated in the region outside the ventricles, and less demarcated in the region of intersection of ventricles and tumor.

Figure 7 shows another example of the capability of the ICF to extract the third dimension from two-dimensional MRI images. As shown inside the white ellipses in (b) and in (d), the third dimension is shown at the location of the white nuances seen in (a) and in (c). Also, looking inside the white ellipses in (b) and in (d) it is discernible the depth of the ventricle from the image plane. Outside the white ellipses the third dimension is well visible also for the rest of the anatomical structures. Particularly, when looking at the image shown in (b), both of the sub-cortical structures and the cerebellum are emphasized. It is interesting to note the reproduction in (b) and in (d) of the tumor structures visible through the white nuances shown in (a) and in (c). Although scattered, the contour line of the tumor is visible in (b), whereas in (d) is distinctively shown.

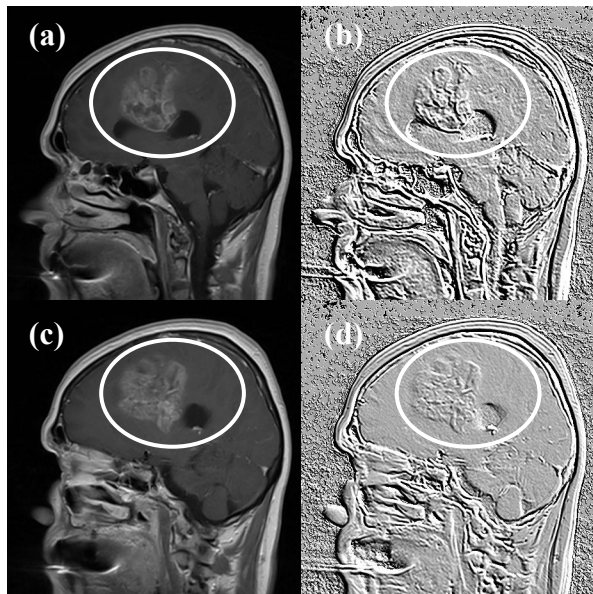


Figure 7. The original MRI images are shown in (a) and in (c) and their corresponding ICF images are shown in (b) and in (d). The pixels matrix size is 512×512 with pixel size of $0.45\text{mm} \times 0.45\text{mm}$. The images were cropped. The white ellipses surround the tumor region along with the ventricle. The third dimension perpendicular to the image plane is visible in (b) and in (d) both inside the ellipses and also outside so to highlight all of the anatomical structures. The contour line of the tumor is visible both in (b) and in (d).

4. Discussion

4.1. The Relevance of the Works within the Context of the Current Literature

Magnetic Resonance Imaging is presently recognized as non-invasive diagnostic technique without harmful side effects [18, 19], and is employed also to diagnose tumors in the human brain [20]. More specifically, Proton Magnetic Resonance Spectroscopy has been reported to be successful in the classification of human brain tumors [21]. To assess the efficacy of the treatment to the human brain tumor and early prediction of treatment response, a non-invasive biomarker (tumor water diffusion) has been reported successful when the tumor is detected with diffusion MRI [22]. Within the context of a technique for pre-surgical human brain tumor quantification, dynamic contrast-enhanced MRI was used in order to quantify tissue fractional blood volume and microvascular permeability [23]. The technique proved to be useful in the assessment of the therapy. In order to investigate the progression of non-enhancing lesions, within the context of human brain tumor diagnosis, Magnetic Resonance Spectroscopic Imaging was reported to be capable to provide additional information to the conventional MRI examination [24]. Diffusion Weighted MRI used along with echo-planar imaging (EPI) proved useful to study the human brain tumor cellularity [25]. Also, the literature reports on Magnetoencephalography (MEG) studies of slow band oscillations [26] and fast band oscillations [27] associated with tumors and epilepsy in the human brain.

Automatic tumor segmentation from MRI images was performed through knowledge-based techniques which use clustering [28], and on the basis of an outlier detection which makes use of three steps: (i) detection of abnormal regions and determination of the intensities of the tissue type, (ii) comparison with T2 images containing the abnormal regions, and (iii) application of geometric and spatial constraints [29]. Also, it was reported an automated brain tumor segmentation which uses a hidden Markov Random field [30]. Automatic segmentation of brain tumor accompanied by neural network classification of the tissue type: normal, benign lesion, and malignant has also been reported [31]. Finally, fractal based methodologies have been reported to detect and segment the tumor from MRI [32, 33]. As far as regards the human brain tumor boundary detection from MRI, a Hopfield neural network was employed [34].

In order to frame the works herein reported into the literature it is necessary to consider the rationale of the study, which is the task of extracting a third dimension from 2D MRI images of a human brain tumor. So far, no studies have been reported attempting to achieve the aforementioned task. The rationale yields to a discovery, which is the capability of the ICF of the MRI to extract the tumor contour line. The task of the extraction of the tumor contour line is well correlated with: (i) tumor segmentation and (ii) tumor volume determination; which are largely addressed in the

literature. Therefore, the aforementioned task is the connection between this research and the literature. Additionally, the methodology used to extract the tumor contour line has been conducted through an approach which is novel in its nature: the extraction of the third dimension from 2D MRI images. As a matter of fact, in the present manuscript, the identification of the tumor margins has been successfully achieved through the use of the Intensity-Curvature Functional of the bivariate linear formula.

4.2. The Originality of the Works within the Context of the Current Literature

The area of research treated in this manuscript is at the intersection between the previously mentioned tasks of: (i) tumor segmentation [2, 10, 12, 28, 30-33], and (ii) tumor volume determination [10, 13]. Such intersection consists in the extraction of the tumor contour line through the mathematical engineering tool called Intensity-Curvature Functional (ICF). Using the ICF is also possible to determine the 2D extension of the tumor because the contour line surrounds the tumoral mass. The outcome of the ICF is not a separated (segmented) tumor volume, neither is the tumor volume as measured through signal processing algorithms. The outcome of the ICF is the contour line of the tumor and the 2D representation of its extension. Current research [35] shows that is possible to retrieve the depths of the anatomical structures of the brain, which is a task correlated with the extraction of the third dimension of 2D MRI (which is a task addressed in literature for the first time). The aforementioned task is possible by the use of the ICF of the cubic trivariate Lagrange model polynomial function [35], however, the most effective behavior is that one of the ICF of the bivariate linear function which is such to extract the third dimension of the 2D MRI in the most remarkable way so far observed.

5. Conclusions

The size of the tumor mass can be enhanced through the use of post-Gd T1-weighted MRI so to determine also the borderline of the active tumor [36]. T2-weighted MRI can be used to quantify the volume of the edema regions surrounding the tumor [37]. Some other imaging modalities such as PET may also be used [38]. The key in the works herein presented is to show that other information can be added to the 2D MRI and such information is collectible through T1-weighted and T2-weighted MRI, by using the ICF of the bivariate linear function. In fact, the present works show that the additional information is the third dimension of the MRI which is made visible in the ICF images, whereas in [35] it has been shown that the combined use of the Classic-Curvature [14] and the ICF [17, 39] may provide complementary and/or additional information to MRI. Also, it is relevant to stress on the clinical and physical meanings of the resultant ICF images. The meaning of the ICF images is in the capability to identify the tumor borderline without

the need of a segmentation algorithm. Furthermore, qualitative comparison has been made in this paper between the original MRI and the ICF images so to show the reliability the ICF images. The present study may constitute a gold standard to be used when comparing MRI and ICF results from other subjects.

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This work presents a case study on a patient suffering from a tumor in the human brain. The MRI scans were collected in agreement with ethical committees of the Skopje City General Hospital. Compliance with the Declaration of Helsinki and the obtainment of the proper informed consent is assured because of the fact that the subject had the original MRI collected for clinical inspection purposes. The software is available from the corresponding author at no charge whatsoever.

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