ISSN: 1992-8645

www.jatit.org



MULTIMODAL PIPELINE FOR QUANTITATIVE METRICS ESTIMATION OF BRAIN TISSUE MICROSTRUCTURE USING DMRI DATA

ABDERRAZEK ZERAII¹, AMINE BEN SLAMA¹, SABRI BARBARIA¹, MOKHTAR MARS¹, CYRINE DRISSI², TAREK KRAIEM³

¹University of Tunis El Manar, ISTMT, LRBTM, LR13ES07, Tunis, Tunisia

²National Institute of Neurologie, Tunis, Tunisia

³Department of Radiology, King Abdulaziz Specialist Hospital in Taif, Saudi Arabia

ABSTRACT

White matter changes in the corticospinal tract (CST) contribute to executive dysfunction in the context of motor control of the body and limbs. The objectives of this study remained to characterize the corticospinal tract using different models for the diffusion MRI signal. We employed the DTI (diffusion tensor imaging) and Multi-Shell Multi-Tissue Constrained Spherical Deconvolution to estimate a multitissue orientation distribution function (ODF) analysis of 10 healthy Subjects. In this paper, our goal is to determine the sensitivity of fibre orientation distribution (FOD) compared to the standard Diffusion Tensor Imaging (DTI) approach and select the FOD-DEC difference existing in the two regions of interest (PLIC and PONS). For each subject, biophysical values were calculated for two Regions of Interest (the posterior limb of the internal capsule and the anterior pons) at two b-value (b=1000s/mm² and b=3000 s/mm²). Experimental results showed that the pons region more accurately predict CST integrity than the posterior limb of internal capsule using a b-value equal to 1000 s/mm². FA and ADC are a promising metric for clinical applications especially when we rely on qualitative data from the CSD model.

Keywords: MRI, Diffusion Tensor Imaging, fibre orientation distribution, Multi-Shell Multi-Tissue, Constrained Spherical Deconvolution (MSMT-CSD).

1. INTRODUCTION

Diffusion-weighted magnetic resonance imaging (DW-MRI) is the only tool to study the brain connectivity and organization non-invasively and in-vivo through a process known as tractography [1]. In the case of brain tissues, we need to perform models that characterize the diffusion and reproduce the preferred directions [2]. The complex model used to characterize diffusion is the Diffusion Tensor model [3] which allows the representation of the anisotropy as an ellipsoid. Many microstructural properties may be extracted from Diffusion Tensor Imaging (DTI) such as Fractional Anisotropy (FA) and Apparent Diffusion Coefficient (ADC). The quantitative indices provided by the DTI technique are exploited by neurologists for the diagnosis of a wide variety of brain pathologies. Commonly, DTI technique has been used to relate changes in white matter microstructural properties and motor function after stroke [4]. The corticospinal tract (CST) is the most important pathway responsible for intact motor functions, it has been widely explored using DTI. Its integrity is essential for preservation of motor functions [5]. FA and ADC assesses how freely water molecules can diffuse and are indicative of the integrity of white matter microstructure. Several methods are currently in use to measure quantitative biophysical parameters in a variety of regions of interest (ROIs) representing the CST with no consensus about which approach is best [6]. Accordingly, we focus in this study on the variability in parameters derived from DTI and we compared the anisotropy of the posterior limb of the internal capsule and the anterior pons between

<u>15th January 2021. Vol.99. No 1</u> © 2005 – ongoing JATIT & LLS

ISSN: 1992-8645

www.jatit.org

healthy subjects. Therefore, the rest of the paper, we first describe the steps of the followed process to obtain the parameters extracted from the Multi-Multi-Tissue Shell Constrained Spherical Deconvolution (MSMT-CSD) to estimate a multitissue orientation distribution function (ODF) for each subject. With the introduction of high angular resolution diffusion-weighted imaging (HARDI) [5], more advanced methods have emerged that better characterize regions with crossing fibre populations. Spherical deconvolution is one such method, enabling the estimation of the so-called fibre orientation distribution (FOD) [7, 8]. As part of this work, we applied a metric, which we call the Fibre Density (FD). The FD is based on the widely used assumption that intra-axonal water is restricted in the radial direction [9, 10].

This paper is organized as follows: Section 2 details the materials and methods. Section 3 is devoted for results and discussions. The conclusions are provided in section 4.

2. MATERIALS AND METHODS

2.1 Data Processing Pipeline

In the Following section, we review the pipeline of the data-processing steps used in our experiments to measure biophysical parameters from diffusion weighted images. We, finally, present real data acquired from ten healthy subjects. **Step 1: pre-processing**

We corrected the diffusion-weighted dataset for eddy current distortions and motion artifacts and adjusted the diffusion gradients with proper rotation of the b-matrix.

Step 2: Brain mask extraction

In order to reduce the computation time, the DW images were masked to eliminate from the parametric computation all the voxels outside the subject brain area. The masking process is done using BET in FSL software [14].

Step 3: Diffusion tensor modeling

In the current study, we performed DTI diffusion model that characterize the diffusion and reproduce the preferred directions in each voxel. In fact, for a neuron, the diffusion is fast along the axon and reduced in the other directions and therefore the distribution of the ADC values of the water in the white matter can be modeled by an ellipsoid whose shape give information about the preferred directions of diffusion [11].

Step 4: Parametric maps calculation

The FA index is appropriately normalized so that it takes values from zero (when diffusion is isotropic) to one (when diffusion is preferred along one axis only). We, also, calculate the mean diffusivity that is defined as the average of the diagonal coefficients of diffusion tensor, it indicates if the diffusion is globally large or restricted.

Step 5: Region of interest (ROI) based analysis

The diffusion anisotropy measurements (FA and ADC values) were averaged across specific Regions of Interest (ROIs). We manually delineate the following two ROIs in each subject: the posterior limb of the internal capsule, and the anterior pontine area.



Fig.1. shows the reverent workflow of the Pipeline when we compute the biophysical parameters.

2.2 Human Connectome Project Diffusion data

We evaluated diffusion imaging measures of the corticospinal tract obtained with a DTI algorithm. In this paper, the data of 10 healthy volunteers are from Human Connectome Project (HCP), which <u>15th January 2021. Vol.99. No 1</u> © 2005 – ongoing JATIT & LLS

www.jatit.org

173

E-ISSN: 1817-3195

can be found on Connectome DB with b = 1000 s/mm² and b = 3000 s/mm². Table 1 summarizes the parameters used data acquisition.

Table 1: Summary of the used parameters for data acquisition.

Parameter	Value
Sequence	Spin-echo EPI
TR/TE (ms)	8800/57
FOV (mm)	210x210
Matrix	1 40x140
Echo spacing (ms)	0.63
Slices	96 slices, 1.5 thick
b-values (s/mm2)	1000,3000
Number of directions	64

The masking process is done using BET in FSL software. We calculated Fractional Anisotropy (FA) and Axial Diffusivity (AD) maps from a tensor model estimated using MRtrix3 software [12]. A two-regions-of-interest approach was used to measure FA and ADC metrics [13]. Statistical test analysis was achieved using the R programing Software (V.2.5019).

2.3 Response function estimation

Different response functions can be estimated for the three different tissue types: white matter (WM), gray matter (GM), and cerebrospinal fluid (CSF) [14]. The shape of this response function is a sphere, which denotes isotropic diffusion. We can already estimate angular resolution and therefore anisotropy of white matter. The angular resolution increases even further for the last two shells (b1000 and b3000).

different response functions b=1000s/mm² different response functions b=3000s/mm²



Fig.2 Tissue-dependent response functions estimated separately for different tissue types. For each tissue type, the response function was estimated from an average of the data of the voxels

2.4 Estimation of Fiber Orientation Distributions (FOD)

Based on the different response functions for the different tissue-types, it is possible to differentiate between those tissue types to estimate the orientation of all fibers crossing that voxel. The FOD could accurately resolve crossing fibers [5].

2.5 Spherical deconvolution

The spherical deconvolution method provides an estimate of the distribution of fibres within each imaging [15]. The method assumes that the measured HARDI signal can be expressed as the convolution over spherical coordinates of a single canonical fibre response function with the fibre © 2005 – ongoing JATIT & LLS

ISSN: 1992-8645

www.jatit.org



E-ISSN: 1817-3195

orientation distribution (FOD). The FOD can then be estimated by performing the reverse spherical deconvolution operation using spherical and rotational harmon [16].

For this work, we use Constrained Spherical Deconvolution (CSD) which places a nonnegativity constraint on the estimated FOD [17]. CSD provides more reliable estimates of the FOD and makes it possible to resolve fibre orientations at more acute angles than is possible without the constraint. Like other higher-order approaches, the spherical deconvolution method benefits from the increased angular contrast provided by high bvalues [18]. In this work we use a two b-value of 1000 s/mm² 3000 s/mm²[19]. Fibre Density (FD) for the analysis of high angular resolution diffusion-weighted images using higher-order information provided by fibre orientation distributions (FODs) computed using spherical deconvolution. FD has the potential to provide specific information regarding differences between populations by identifying not only the location, but also the orientations along which differences exist. The FOD amplitude is primarily sensitive to the partial volume fraction of the underlying fibre populations. However, previous studies have demonstrated that differences between the actual fibre response function and the assumed response function may also alter the FOD amplitude, but not its orientation [20].

Deviations from the assumed response function may occur during pathology or abnormal development. For example, an increase in radial diffusivity is often associated with white matter pathologies such as axon degeneration and demyelination [21]. Employing an identical response function to compute FODs in different pathologies, causes differences in diffusivity to be reflected as differences in the FOD amplitude.



Fig.3. Quality check of Fiber Orientation Distribution (FOD) estimation.

2.6 FD-specific pre-processing steps

Fixels have been used in the field of Diffusion MRI for a long time: multi-tensor fitting, ball-and-sticks, any diffusion model that is capable of fitting multiple anisotropic elements to each image voxel, can be considered as estimating fixels. However, in the past, researchers have resorted either to lengthy descriptive labels to express the nature of the data being manipulated, or have adopted existing terms, which can lead to confusion with the original sense of the terms. Explains how to perform fixel-based analysis of fibre density and cross-section using single-tissue spherical deconvolution. We note that high b-value (>2000s/mm²) data is recommended to aid the interpretation of apparent fibre density (FD) being related to the intra-axonal space [22].

Fixel-based analysis steps

The diffusion images underwent preprocessing, including corrections for head motion, eddycurrent distortions, susceptibility distortions and intensity inhomogeneities using the FMRIB

<u>15th January 2021. Vol.99. No 1</u> © 2005 – ongoing JATIT & LLS

ISSN: 1992-8645

www.jatit.org

Diffusion Toolbox (FMRIB, Oxford, UK) [23]. Global intensity normalization was performed across participants using tools implemented in MRtrix3 [24]. Next, a group response function was calculated from all participants fibre response functions, which reflect the signal that would be expected from a voxel containing a single, typical fibre bundle [25]. Data preprocessing included removal of noise bias. The noise removal was performed by identifying the noise_ only principal components for local neighborhoods of voxels [26]. Gibb's ringing correction was performed by re_ interpolating the image [27] and eddy current induced distortions were corrected using the FSL toolbox [28].

Segment FOD images to estimate fixels and their apparent fibre density (FD)

Here, we segment each FOD lobe to visualize the orientation of fixels in each voxel.



Fig.4 Fixel-based analysis in the PLIC ROI.

ROIs can be drawn manually on FA, or ADC images. They can be placed on predetermined anatomic regions. In the WM, the homogenous

signal and EPI distortions might impair robust anatomical delimitation of ROI and reproducibility. Basic steps of ROI processing are:

- 1 Registration to improve delineation and to align corresponding voxels in different datasets.
- 2 Normalization to allow standardized localization and comparisons between subjects within a study. For instance, data from each subject can be transferred to standard space, using a validated template or atlas (such as MNI). The choice of the atlas involves checking whether characteristics of the subjects in each study are comparable to those of the subjects scanned to build the template.
- 3 Definition of the ROI manually. Manual delineation can be achieved by free-hand drawing, by placement of basic shapes such as circles/squares or by drawing of the region. In the former, ROI size differs between subjects while in the latter, it remains constant. Small ROIs may be more specific, but also more prone to errors while large ROIs may be less specific for definition of particular structures.
- 4 Manual segmentation has high precision but has disadvantages such as the risk of low reproducibility due to dependence on prior knowledge of the researcher and the lack of feasibility of use in large datasets. Semiautomated delimitation can be a useful alternative by combining the automated identification of the ROI with a interactive selection manual, and modification by the user. Although fully automated delimitation is promising, such as reported by Ohno et al. [29], more studies with large datasets in different phases of stroke are advisable to create a state-of-art automatic method [30].

<u>15th January 2021. Vol.99. No 1</u> © 2005 – ongoing JATIT & LLS

ISSN: 1992-8645

<u>www.jatit.org</u>

E-ISSN: 1817-3195

- 5 Quality control involves assessment of accuracy of segmentation and registration; report of intra- and interrater reliabilities of ROI delineation; clarity of criteria for the location of the ROI such as anatomical location [31].
- 6 Extraction of DTI metrics from the ROI, as absolute values from the site.
- 7 When more than one ROI is chosen, the correction for multiple comparisons is recommended to reduce false positives.

DEC-map	Zoom in Pons
Directions-map	Zoom in Pons
Fiber Density -map	Zoom in Pons
Index-map	Zoom in Pons

Fig.5 Fixel-based analysis steps in the Pons ROI.

3. RESULTS AND DISCUSSIONS

A quantitative summary of the group means and standard deviations corresponding fractional anisotropy (FA) and ADC results on the ten healthy subjects is provided in table 2.

DTI	b	FA	ADC (mean
Parameters	value	(mean	±SD)
		±SD)	
PLIC	1K	0.639±0.	0.0005644±6.92
		0932	6e-05
	3K	$0.57054\pm$	0.0003986 ± 2.67
		0.1004	64e-05
PONS	1K	0.165±0.	0.00102 ± 0.0004
		0932	45
	3K	0.1772±0	0.0006222 ± 0.00
		.123	01398

Table 2: DTI Parameters in Regions of Interest in $b=1000 \text{ s/mm}^2$.

DTI quantitative results of the two parametric metrics (FA, ADC) derived from the DTI model, calculated in two Region of Interest (PLIC, PONS) at two b value (b=1000 s/mm² and b=3000 s/mm²).

As can be appreciated from fig.6, overall FA values in the pons and using b-value 1000 s/mm² have a high level of agreement with each other. The mean FA value is equal to 0.1658. This figure indicates the high correlation between the FA values of the ten subjects in the pons region. In fig.7 a good correlation is found in the pons region and the mean ADC value at the pons at b-value 1000 s/mm² is equal to 0.00189.





Fig.6 Box plot representing the FA values in the PLIC and the pons regions for two b-values.

015

015

and the pons for the two b-value

DTI and CSD metrics varied in different tissue types shown that the pattern of DTI and CSD metrics varied in different tissue types, Voxel-based analysis of FA and ADC in DTI model and FOD estimation from the Multicell Multi-Tissue Constrained Spherical Deconvolution (MSMT-CSD) is a promising new tool for characterizing white matter degeneration. Visualization of FODs and parametric maps derived from DTI model in the specific regions of interest in the healthy subject provide a good marker to analyze the corticospinal tract. The investigation of DTI parameters such as Fractional Anisotropy (FA), that can reflect the fiber density, axonal diameter and myelination in white matter and Apparent Diffusion Coefficient (ADC) that present a quantitative biophysical parameter, these two parameters providing a good biomarker concerning the structural integrity in the

<u>15th January 2021. Vol.99. No 1</u> © 2005 – ongoing JATIT & LLS



www.jatit.org

analyzed ROIs. For voxel-specific approach, a FOD map was obtained by Multi-Shell Multi-Tissue Constrained Spherical Deconvolution (MSMT-CSD) for non-white matter tissues. Interpreting population differences in DTI derived scalar measures such as FA or tensor eigenvalues is challenging in regions with crossing fibres [19],[20],[21]. In this work we applied the Fibre Density, that uses higher-order information provided by FODs to investigate population differences not only in space but also over orientation. This enables differences to be attributed to a single fibre bundle in a region containing multiple fibre populations. As demonstrated by the qualitative analytical simulations shown in Fig. 4, the FOD amplitude is sensitive to the volume fraction of the underlying fibre populations, and to deviations of the actual response function from its assumed form. As shown in Fig.5, FD is primarily affected when the actual and assumed response functions differ along radial orientations, with changes along axial orientations having minimal impact. This is due to the shape of the response function: for a single fibre bundle, the DW signal is highest when measured across the fibres, and strongly attenuated when measured along them, especially at high b-values. An important consideration in estimating the FODs is the choice of fibre response function. In this study, the response function was computed by averaging the response function estimated from all subjects. We also note that differences in the response function will only affect the amplitude of the estimated FODs.

4. CONCLUSIONS

This work introduces a comparative result between two metrics (FA and ADC) in two regions of interest (PLIC and pons) at two b-value (b=1000 s/mm² and b=3000 s/mm²) in healthy subjects. We found that they did not yield identical results. The main finding from this study is that the quantitative biophysical parameter FA and ADC in the pons region are a good biomarker concerning the structural integrity of CST tract, we have also shown that the pattern of DTI and CSD metrics varied in different tissue types. Voxel-based analysis of FA and ADC in DTI model and FOD estimation from the Multi-Shell Multi-Tissue Constrained Spherical Deconvolution (MSMTCSD) is a promising tool for characterizing white matter degeneration. In Future work, we can involve an extensive validation study on several subjects and testing the accuracy of the proposed framework using complex diffusion models. It will be also

interesting to test metrics extracted from tractography in pons region.

REFRENCES:

- Glasser MF., Sotiropoulos, S. N., Wilson J.A., Coalson T. S., Fischl, B., Andersson J. L., et al. (2013). The minimal preprocessing pipelines for the Human Connectome Project. NeuroImage, 80, 105–124.
- [2] Mori, S.: Introduction to Diffusion Tensor Imaging. Elsevier (2007).
- [3] Glasser MF., Sotiropoulos, S. N., Wilson J.A., Coalson T. S., Fischl, B., Andersson J. L., et al. (2013). The minimal preprocessing pipelines for the Human Connectome Project. NeuroImage, 80, 105–124.
- [4] Sharma, N., & Cohen, L. G. (2012). Recovery of motor function after stroke. Developmental psychobiology, 54(3), 254262.
- [5] Lefaucheur, J. P., & Picht, T. (2016). The value of preoperative functional cortical mapping using navigated TMS. Neurophysiologie Clinique/Clinical Neurophysiology, 46(2), 125-133.
- [6] Jayaprakash, N., Wang, Z., Hoeynck, B., Krueger, N., Kramer, A., Balle, E., ... & Blackmore, M. G. (2016). Optogenetic interrogation of functional synapse formation by corticospinal tract axons in the injured spinal cord. Journal of Neuroscience, 36(21), 5877-5890.
- [7] Bosco, E., Peerlings, R. H., & Geers, M. G. (2015). Predicting hygro-elastic properties of paper sheets based on an idealized model of the underlying fibrous network. International Journal of Solids and Structures, 56, 43-52.
- [8] Smith, R. E., Tournier, J. D., Calamante, F., & Connelly, A. (2015). SIFT2: Enabling dense quantitative assessment of brain white matter connectivity using streamlines tractography. Neuroimage, 119, 338-351.
- [9] Raffelt, D., Tournier, J. D., Rose, S., Ridgway, G. R., Henderson, R., Crozier, S., ... & Connelly, A. (2012). Apparent fibre density: a novel measure for the analysis of diffusionweighted magnetic resonance images. Neuroimage, 59(4), 3976-3994.
- [10] Raffelt, D. A., Tournier, J. D., Smith, R. E., Vaughan, D. N., Jackson, G., Ridgway, G. R.,

ISSN: 1992-8645	ISSN:	1992-8645
-----------------	-------	-----------

www.jatit.org

& Connelly, A. (2017). Investigating white matter fibre density and morphology using fixel-based analysis. Neuroimage, 144, 58-73.

- [11] Smith, S. M., Jenkinson, M., Woolrich, M. W., Beckmann, C. F., Behrens, T. E., Johansen-Berg, H., ... & Niazy, R. K. (2004). Advances in functional and structural MR image analysis and implementation as FSL. Neuroimage, 23, S208S219.
- [12] Forse, A. C., Gonzalez, M. I., Siegelman, R. L., Witherspoon, V. J., Jawahery, S., Mercado, R., ... & Long, J. R. (2018). Unexpected diffusion anisotropy of carbon dioxide in the metal organic framework Zn2 (Dobpdc). Journal of the American Chemical Society, 140(5), 1663-1673.
- [13] Woo, J., Lee, J., Murano, E. Z., Xing, F., Al-Talib, M., Stone, M., & Prince, J. L. (2015). A high-resolution atlas and statistical model of the vocal tract from structural MRI. Computer Methods in Biomechanics and Biomedical Engineering: Imaging & Visualization, 3(1), 47-60.
- [14] Dao, T. T., Pouletaut, P., Robert, L., Aufaure, P., Charleux, F., & Ho Ba Tho, M. C. (2013). Quantitative analysis of annulus fibrosus and nucleus pulposus derived from T2 mapping, diffusion-weighted and diffusion tensor MR imaging. Computer Methods in Biomechanics and Biomedical Engineering: Imaging & Visualization, 1(3), 138-146.
- [15] Fernandez, J., Mithraratne, K., Alipour, [24] Andersson, J. L., & Sotiropoulos, S. N. (2016). An integrated approach to correction for off-resonance effects and subject movement in diffusion MR imaging. Neuroimage, 125, 1063-1078. M., Handsfield, G., Besier, T., & Zhang, J. (2018). Towards rapid prediction of personalised muscle mechanics: integration with diffusion tensor imaging. Computer Methods in Biomechanics and Biomedical Engineering: Imaging & Visualization, 1-9.
- [16] Kamagata, K., Zalesky, A., Hatano, T., Di Biase, M. A., El Samad, O., Saiki, S., ... & Hattori, N. (2018). Connectome analysis with diffusion MRI in idiopathic Parkinson's disease: Evaluation using multi-shell, multitissue, constrained spherical deconvolution. NeuroImage: Clinical, 17, 518-529.
- [17] Sinke, M. R., Otte, W. M., Christiaens, D., Schmitt, O., Leemans, A., van der Toorn, A., ... & Dijkhuizen, R. M. (2018). Diffusion MRIbased cortical connectome reconstruction: dependency on tractography procedures and

neuroanatomical characteristics. Brain Structure and Function, 223(5), 2269-2285.

- [18] Schilling, K., Janve, V., Gao, Y., Stepniewska, I., Landman, B. A., & Anderson, A. W. (2016). Comparison of 3D orientation distribution functions measured with confocal microscopy and diffusion MRI. Neuroimage, 129, 185-197.
- [19] Fan, Q., Witzel, T., Nummenmaa, A., Van Dijk, K. R., Van Horn, J. D., Drews, M. K., ... & Hedden, T. (2016). MGH– USC Human Connectome Project datasets with ultra-high bvalue diffusion MRI. Neuroimage, 124, 1108-1114.
- [20] Dhollander, T., Raffelt, D., & Connelly, A. (2017). Towards interpretation of 3-tissue constrained spherical deconvolution results in pathology. 25th International Society of Magnetic Resonance in Medicine, 25, 1815.
- [21] Schilling, K. G., Janve, V., Gao, Y., Stepniewska, I., Landman, B. A., & Anderson, A. W. (2018). Histological validation of diffusion MRI fiber orientation distributions and dispersion. Neuroimage, 165, 200-221.
- [22] Campbell, G., & Mahad, D. J. (2018).
 Mitochondrial dysfunction and axon degeneration in progressive multiple sclerosis.
 FEBS letters, 592(7), 1113-1121.
- [23] Kunz, N., da Silva, A. R., & Jelescu, I. O. (2018). Intra-and extra-axonal axial diffusivities in the white matter: Which one is faster?. Neuroimage, 181, 314-322.
- [24] Andersson, J. L., & Sotiropoulos, S. N. (2016). An integrated approach to correction for offresonance effects and subject movement in diffusion MR imaging. Neuroimage, 125, 1063-1078.
- [25] Tournier, J. D., Smith, R., Raffelt, D., Tabbara, R., Dhollander, T., Pietsch, M., ... & Connelly, A. (2019). MRtrix3: A fast, flexible and open software framework for medical image processing and visualisation. NeuroImage, 116137.
- [26] Mazian, B., Bergeret, A., Benezet, J. C., & Malhautier, L. (2018). Influence of field retting duration on the biochemical, microstructural, thermal and mechanical properties of hemp fibres harvested at the beginning of flowering. Industrial Crops and Products, 116, 170-181.
- [27] Ohno, Y., Koyama, H., Nogami, M., Takenaka, D., Matsumoto, S., Yoshimura, M., ... & Sugimura, K. (2007). Postoperative lung function in lung cancer patients: comparative analysis of predictive capability of MRI, CT, and SPECT. American Journal of Roentgenology, 189(2), 400-408.

<u>15th January 2021. Vol.99. No 1</u> © 2005 – ongoing JATIT & LLS

ISSN: 1992-8645	www.jatit.org	E-ISSN: 1817-3195

- [28] Smith, E. E., Kent, D. M., Bulsara, K. R., Leung, L. Y., Lichtman, J. H., Reeves, M. J., ... & Zahuranec, D. B. (2018). Accuracy of prediction instruments for diagnosing large vessel occlusion in individuals with suspected stroke: a systematic review for the 2018 guidelines for the early management of patients with acute ischemic stroke. Stroke, 49(3), e111-e122.
- [29] Froeling, F. E., Feig, C., Chelala, C., Dobson, R., Mein, C. E., Tuveson, D. A., ... & Kocher, H. M. (2011). Retinoic acid–induced pancreatic stellate cell quiescence reduces paracrine Wnt–β-catenin signaling to slow tumor progression. Gastroenterology, 141(4), 1486-1497.
- [30] Dijkhuizen, R. M., Singhal, A. B., Mandeville, J. B., Wu, O., Halpern, E. F., Finklestein, S. P., ... & Lo, E. H. (2003). Correlation between brain reorganization, ischemic damage, and neurologic status after transient focal cerebral ischemia in rats: a functional magnetic resonance imaging study. Journal of Neuroscience, 23(2), 510-517.
- [31] McGraw, T., & Guayaquil-Sosa, A. (2018). Hybrid rendering of exploded views for medical image atlas visualization. Computer Methods in Biomechanics and Biomedical Engineering: Imaging & Visualization, 6(6), 668677.