Macular Lesions Extraction Using Active Appearance Method

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Abstract. Age-related macular degeneration (ARMD) is one of the most widespread diseases of the eye fundus and is the most common cause of vision loss for those over the age of 60. There are several ways to diagnose ARMD. One of them is the Fundus Autofluorescence (FAF) method, and is one of the modalities of Heidelberg Engineering diagnostic devices. The BluePeakTM modality utilizes the fluorescence of lipofuscin (a pigment in the affected cells) to display the extent of the disease's progression. In clinical practice is often quite complicated to perform assessment of precise parameters macular lesions. The main aim of the article is design of the method which is able to locate and consequently perform extraction of these lesions. The algorithm body is composed of several essential parts: image preprocessing, filtration of interested area and segmentation procedure. In the first step, extraction area of interest is performed. Filtration process should suppress adjacent structures. Final step is segmentation procedure. The main advantage is that the whole process is fully automatic. The result of segmentation is closed curve which is formed iteratively to edges of analyzed object. The resulting curve reflects geometrical parameters of analyzed structure. On the base this fact is quite easy to calculate perimeter and area of analyzed area.

Keywords: Macular degeneration · Optical coherence tomography · Image processing · Active contour · Medical image segmentation · MATLAB · Geometrical parameters · Macular lesions

1 Introduction

Reticular macular lesions, also known as 'reticular macular disease', 'reticular drusen', 'reticular pseudodrusen', or 'subretinal drusenoid deposits', are a pattern of lesions commonly found in age-related macular degeneration and best visualized using at least two imaging techniques in combination. Reticular lesions have four stages of progression observable on spectral domain optical coherence tomography, but they do not show the usual signs of regression of soft drusen (calcification and pigment changes). Furthermore, reticular lesions correlate histologically with subretinal drusenoid deposits localized between the retinal pigment epithelium and the inner segment ellipsoid band. Reticular

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lesions are most commonly seen in older age groups of female patients with age related macular degeneration and are usually bilateral. They are not clearly associated with known age-related macular degeneration genes and are highly associated with late-stage age-related macular degeneration and an increased mortality rate. They are also associated with alterations in the neural retina and choroid [1–3, 16] (Fig. 1).

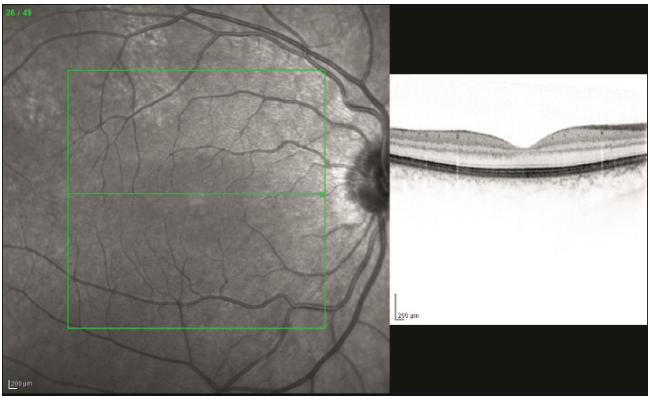

Fig. 1. Cut of area physiological macula with using infrared shootings (left) and OCT cut (right) [1].

2 Age-Related Macular Degeneration

Age-related macular degeneration is a major cause of blindness worldwide. With ageing populations in many countries, more than 20 % might have the disorder. Advanced age-related macular degeneration, including neovascular age-related macular degeneration (wet) and geographic atrophy (late dry), is associated with substantial, progressive visual impairment. Major risk factors include cigarette smoking, nutritional factors, cardiovascular diseases, and genetic markers, including genes regulating complement, lipid, angiogenic, and extracellular matrix pathways. Some studies have suggested a declining prevalence of age-related macular degeneration, perhaps due to reduced exposure to modifiable risk factors. Accurate diagnosis combines clinical examination and investigations, including retinal photography, angiography, and optical coherence tomography. Dietary anti-oxidant supplementation slows progression of the disease. Treatment for neovascular age-related macular degeneration incorporates intraocular injections of anti-VEGF agents, occasionally combined with other modalities. Evidence suggests that two commonly used anti-VEGF therapies, ranibizumab and bevacizumab, have similar efficacy, but possible differences in systemic safety are difficult to assess. Future treatments include inhibition of other angiogenic factors, and regenerative and topical therapies [1, 2, 4–6] (Fig. 2).

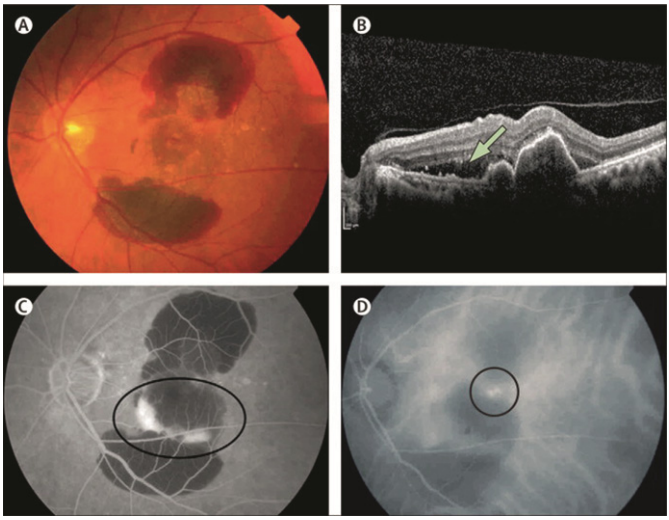

Fig. 2. Patient with polypoidal choroidal vasculopathy. (A) Fundus photograph showing massive subretinal haemorrhage and exudation with (B) corresponding subretinal thickening and elevation (arrow) on optical coherence tomography. (C) Corresponding fluorescein angiogram showing ill-defined "occult" pattern leakage (circled), whereas the indocyanine-green angiogram (D) shows discrete polypoidal lesions under the fovea (circled) [1].

3 Optical Coherence Tomography (OCT)

OCT is a laser device that employs a superluminiscent diode as the source of its coherent beam. This diode emits a beam of a suitable wavelength into the eye structure; the beam is reflected by various layers of the retina and interferes with a second reference beam in a detector. The resulting interference signal is then digitized and used to obtain the final image. For developing a method for automatically calculating macular lesions, we used images acquired by a Spectralis unit from Heidelberg Engineering [8–11].

3.1 Blue Laser Auto Fluorescence

One modality of OCT devices is BluePeakTM, which excites the ocular fundus (fundus oculi) with a blue spectrum laser beam ($\lambda = 488$ nm). This modality is most commonly used for diagnosing macular degeneration due to the presence of lipofuscin, which is a specific source of fluorescence. During the examination, the beam is shot into the patient's eye where it induces lipofuscin fluorescence that is caught by the detector and subsequently analysed. The main advantage is the possibility of comparison with OCT results that provide information on the morphological changes in the retinal pigment epithelium (RPE), while BluePeak^{TM} shows metabolic changes [7, 12–16].

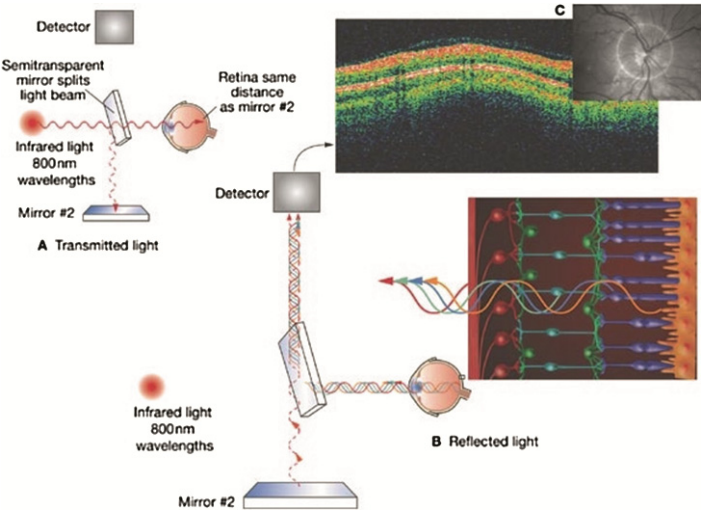

Fig. 3. High-resolution images of the internal retinal structure taken with optical coherence tomography (OCT) [1]

4 The Proposed Solution for Automatic Extraction of Macular Lesions and Geometrical Parameters

As it is mentioned above, analysis of macular lesions is for clinical practice very important. Currently, ophthalmological physicians for many cases must perform analysis and clinical diagnosis of macular lesions only by their eyes. The main intention of proposed software solution is improving and mainly validating of diagnosis macular lesions. In terms of macular lesion diagnosis is the most important extraction of geometrical parameters. Especially it is needed to obtain closed area of macular lesion and consequently area of this contour. At the beginning of algorithm ophthalmologic records are loaded. In the next step it is necessary to perform preprocessing of records. This part includes filtration process by average filter and image resizing. For our purpose is used average filter of dimension 4×4. After that the center of macular lesion is set. Segmentation procedure is done in iterative steps. Using of more iterative steps give the elaborated shape of final contour but on the other hand it increases computational time of whole process. Because of it, it is used compromise of 100 iterative steps which reliably reach contour of macular lesion. In the final step it is computed number of pixels which are placed inside the contour (Fig. 4).

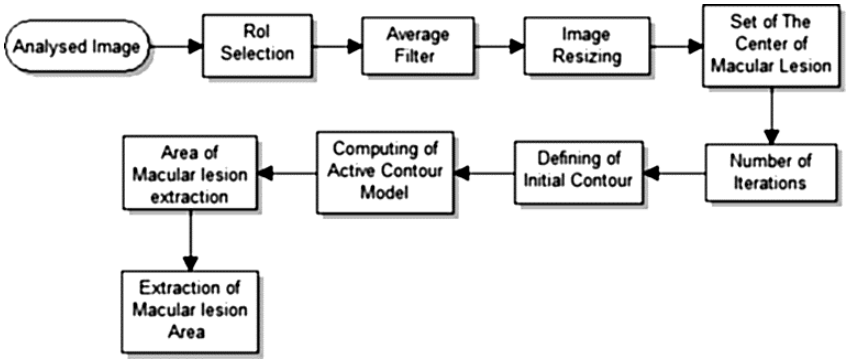

Fig. 4. The proposed algorithm for analyzing of macular lesions

4.1 The Principle of Active Contour Method

Used type of geometrical contour is derived from implicit equation of initial curve. For purposes of our analyses circle with zero shift is used:

$$x^2 + y^2 = r^2 \rightarrow x^2 + y^2 - r^2 = 0 \tag{1}$$

Initialization function is formed in individual iteration steps to shape of macular lesion. On level set method, analyzed image is divided by contour into inside and outside part. Image is composed from three parts: Inside area is consist by negative values (negative values of shortest Euclidean distance of points from contour). Inside area (positive value of the shortest Euclidean distance points from contour) and contour with zero value. The further away from the point of the curve, the larger the resulting value. The result of this procedure is the cone which defines the distance the positive and negative values from zero, and thereby to form level set area. Level set area is defined by level set function Φ which is given by following equation:

$$\Phi(x, y, t) \tag{2}$$

Value range of function Φ is placed to $\mathbb{R}^3$. It is not just curve, but whole domain is defined which is consecutive changed by the time. For the simplest case for defining level set evolution it is necessary to define gradient. Gradient is needed for performing proper evolution of level set area:

$$\nabla\Phi = \left(\frac{\partial\Phi}{\partial x}, \frac{\partial\Phi}{\partial y} \right) \tag{3}$$

Evolution of level set by the time is given by partial derivation level set function Φ by the time $\frac{\partial\Phi}{\partial t}$.

Final contour is formed by the time in the direction of normal when velocity of evolution "c" is being stable.

$$\frac{\partial \Phi}{\partial t} = c.N \tag{4}$$

Normal vector is given by relationship:

$$N = \frac{\nabla \Phi}{|\nabla \Phi|} \tag{5}$$

Direction of normal is determined by gradient. Normal vector is vertical to tangent of contour which is developed in direction of this normal multiplied by constant. Instead of constant velocity we can use function divergence of normal. Divergence function determines when vectors converge to some particular point. In the first step normal and divergences are calculated. Negative divergence denotes on convergence of vectors. Evolution of level set area is performed by this approach. This level set area is independent on image values.

The most frequently used contours are based on principle of minimization of energy functional. Functional is representation which assigns real number. Contour is placed in functional and its size of energy is controlled. If the energy is too large, the contour is gradually deformed into a shape that reduces energy. This procedure is performed until we reach energy minimization. Active contour method is iterative algorithm, which forms final contour in consecutive steps. The key parameter is number of those steps. We must keep perimeter of analyzed object. For our purpose 100 iterations have been used for reaching shape of macular lesions [13, 16–19].

5 Analysis of Macular Lesions

For testing of the designed software, 40 patient's records of macular lesions have been used. Testing has been performed with same requirement and its background suppression and reaching of final contour macular lesion. Segmentation gave satisfactory results for 35 patients. On the rest images we had problems with adjacent blood vessels which we are not able to suppress. This fact causes worse effectivity of detection. Images obtained through the BluePeak modality provide unique information about the condition of macular degeneration and its terminal stage – geographic atrophy. Thanks to these high contrast images, it is possible to determine the geometric parameters of macular lesions. For the subsequent processing of native images, we used the MATLAB® interactive programming environment. The aim was to quantify the area of the ocular fundus of macular lesions. This geometric parameter allows clinicians to clarify and predict the further development of the disease. Emphasis was particularly placed on those segmentation methods that allow for an automated analysis. The geometric active contours driven by local Gaussian distribution fitting energy method – one of the level-set segmentation procedures – proved to be the best. The algorithm is divided into several basic parts. First, the patient's image is loaded into the device and the macular lesion

zone is framed; calculation of the macular lesion area follows. The selection of the macular lesion area (in Fig. 3) is indicated using the active contour model (the gradual shaping of contours up to the edge of the object in the image). With zero approximation, the contour is defined as initial circle whose size is consecutively adapted to the size of the lesion. After the contour completes the segmentation, the number of pixels contained therein is calculated. Here we use the properties of level-set methods that divide the image into two parts: the part inside the contour and the part outside the contour. The contour corresponds to zero values. The sum of the number of pixels is defined by a cycle that evaluates all the pixels in the contour as being logical ones. The conversion of the number of pixels per unit area occurs via image resolution. In Heidelberg Spectralis OCT devices, this resolution corresponds to 200 μm. The resulting geometric parameter, i.e. the size of lesion area, is $S = 7.156\ mm^2$ in the first case (in Fig. 3c) and $S = 8.9796\ mm^2$ in the latter case (in Fig. 3f). A current shortfall of this analysis is the vascular bed, which is one of the most contrasted parts of the ocular fundus and the active contour extends behind it. Further development of this method should focus on subtracting the area of the vascular bed, which will significantly improve the diagnosis of retinal disease [16] (Fig. 5).

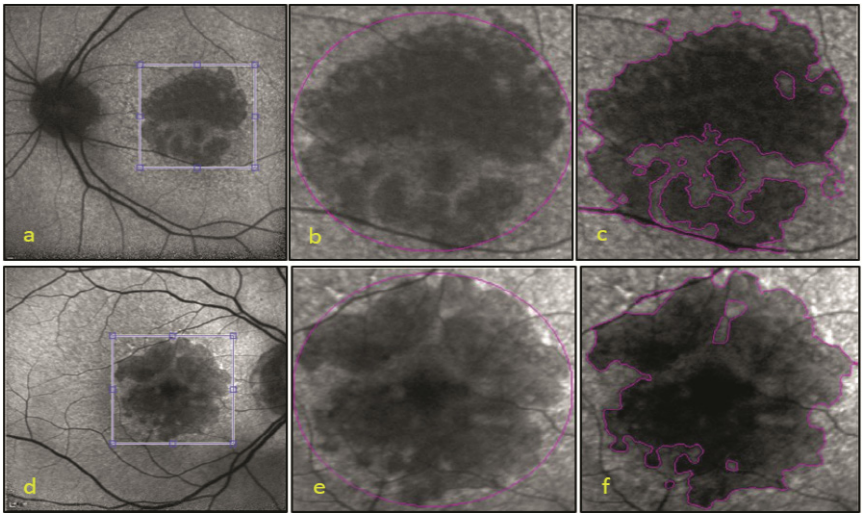

Fig. 5. Selection of macular lesion area (a, d), the contour's initial state before segmentation process (b, e) and resulting segmentation outputs (c, f) [16].

6 The Design of Application GA ANALYSIS

The final result of analysis is function application which is intended for using in clinical practice. The function of application is presented in the following patient's record. 91 years old patient with geographical atrophy, placed in left eye. Infrared image and OCT

is shown in Fig. 6. For this particular case it is obtained the fundus diameter 8808 μm. The working environment of OCT Spectralis is shown in Fig. 6. On the infrared image, there are marked spots where OCT cuts are performed. One of them is in the right part of the image. There is also visible the ablation of retinal layers in the area of geographic atrophy (Fig. 7).

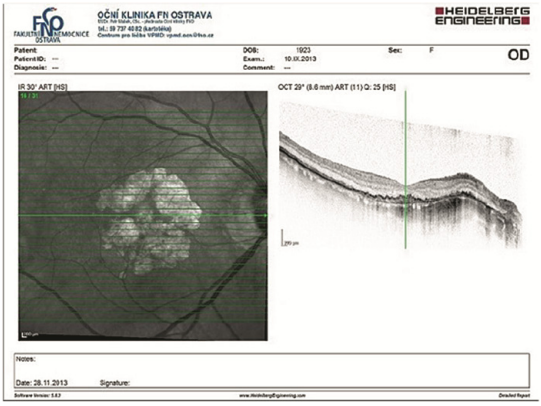

Fig. 6. The working environment of OCT Spectralis. IR image of right eye (left) and OCT cut by disordered macula (right)

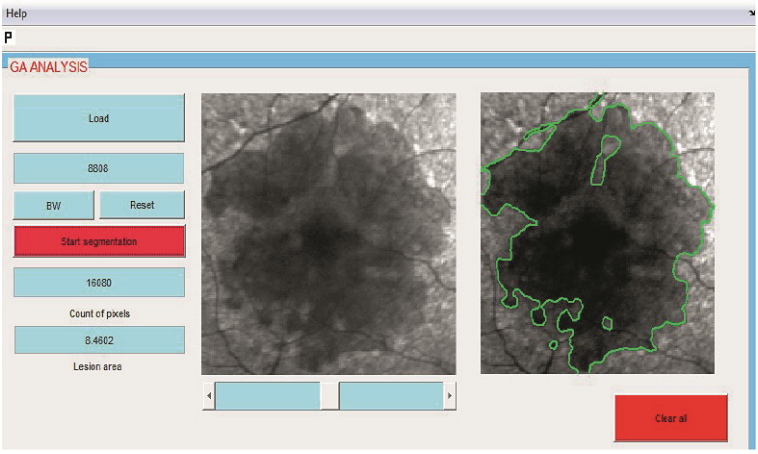

Fig. 7. The working environment of software GA ANALYSIS

7 Conclusion

Analysis of macular lesions is very important task in the field of ophthalmologic. In clinical practice it is important automatic method for assessing of macular lesion area

and consequent evaluation of geometrical parameters. The proposed software solution offers appropriate way for automatic extraction of macular lesion and geometrical parameters as well. The proposed software solution has been tested on the sample of 40 patient's records. In the algorithm output image data are loaded. After that segmentation procedure is performed by active contour method. This method is going in iteration steps. For our purposes it is used 100 iterative steps. In the case of using larger number of iterations, we may use the more elaborate shape of analyzed object. On the other hand it would increase computation time of whole segmentation process. The significant problem of detection macular lesion is presence of adjacent blood vessels on the analyzed images. If we did not suppress those structures, active contour would spread out of analyzed object and whole segmentation process would be deteriorated. Due this fact, average filter is used. On the base low pass filtration it is possible to partially suppress adjacent structures and highlight area of macular lesions. In the present time the proposed software is being tested in clinical practice. Software results are being compared with opinions of ophthalmologic physicians from University hospital of Ostrava. There is one unfavorable fact witch deal with adjacent structures of analyzed records. In some cases it is complicated to suppress adjacent blood vessels in order to achieve more precise detection of macular lesion. In the coming time we want to focus on developing model of macular lesion which completely suppress those structures and process of detection will be more effective.

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References

1. Wang, Z.L., et al.: Bevacizumab cured age-related macular degeneration (AMD) via down-regulate TLR2 pathway. Cent. Eur. J. Biol. **9**(5), 469–475 (2014). doi:10.2478/s11535-014-0290-5
2. Christen, W.G., Chew, E.Y.: Does long-term aspirin use increase the risk of neovascular age-related macular degeneration? Expert Opin. Drug Saf. **13**(4), 421–429 (2014). doi:10.1517/14740338.2014.889680
3. Pustkova, R., et al.: Measurement and calculation of cerebrospinal fluid in proportion to the skull. In: 2010 9th Roedunet International Conference (RoEduNet) (2010)
4. Cheung, L.K., Eaton, A.: Age-related macular degeneration. Pharmacother. J. Hum. Pharmacol. Drug Ther. **33**(8), 838–855 (2013). doi:10.1002/phar.1264
5. Penhaker, M., Matejka, V.: Image registration in neurology applications. In: 2010 International Conference on Networking and Information Technology (ICNIT) (2010)
6. Tsika, C., Tsilimbaris, M.K., Makridaki, M., Kontadakis, G., Plainis, S., Mos-chandreas, J.: Assessment of macular pigment optical density (MPOD) in patients with unilateral wet age-related macular degeneration (AMD). Acta Ophthalmol. **89**(7), e573–e578 (2011)

7. Besirli, C.G., Comer, G.M.: High-resolution OCT imaging of RPE degeneration in bilateral diffuse uveal melanocytic proliferation. Ophthalmic Surg. Lasers Imaging **41**(6), S96–S100 (2010). doi:10.3928/15428877-20101031-03
8. Stetson, P.F., et al.: OCT Minimum intensity as a predictor of geographic atrophy enlargement. Invest. Ophthalmol. **55**(2), 792–800 (2014). doi:10.1167/iovs.13-13199
9. Alam, S., et al.: Clinical application of rapid serial fourier-domain optical coherence tomography for macular imaging. Ophthalmology **113**(8), 1425–1431 (2006). doi:10.1016/j.ophtha.2006.03.020
10. Kubicek, J., et al.: Segmentation of MRI data to extract the blood vessels based on fuzzy thresholding. In: Barbucha, D., Nguyen, N.T., Batubara, J. (eds.) New Trends in Intelligent Information and Database Systems, pp. 43–52. Springer International Publishing, Heidelberg (2015)
11. Coscas, G., et al.: Optical Coherence Tomography in Age-Related Macular Degeneration: OCT in AMD. Springer, Heidelberg (2009). ISBN: 978-364-2014-680
12. BLUE LASER AUTOFLUORESCENCE. A supplement to Ophthalmology Times Europe: Blue Laser Autofluorescence. Advanstar Communications, Chester, UK [cit. 2013-12-03] (2009). ISSN: 1753-3066
13. Wang, L., et al: Active contour driven by local Gaussian distribution fitting energy. Sig. Process. **89**(12), 2435–2447 (2009). doi:10.1016/j.sigpro.2009.03.014
14. Kubicek, J., Penhaker, M.: Fuzzy algorithm for segmentation of images in extraction of objects from MRI. In: 2014 International Conference on Advances in Computing, Communications and Informatics (ICACCI 2014). IEEE (2014)
15. Kodaj, M., Kubicek, J., Penhaker, M., Bryjova, I.: Articular cartilage defect detection based on image segmentation with colour mapping. In: Hwang, D., Jung, J.J., Nguyen, N.-T. (eds.) ICCCI 2014. LNCS, vol. 8733, pp. 214–222. Springer, Heidelberg (2014)
16. Kubicek, J., Bryjova, I., Penhaker, M., Javurkova, J., Kolarcik, L.: Segmentation of macular lesions using active shape contour method. In: The 1st European-Middle Asian Conference on Computer Modelling, Issyk Kul, Kyrgyzstan, 25–27 August 2015
17. Krawiec, J., Penhaker, M., Novák, V., Bridzik, R., Kasik, V.: User interactive biomedical data web services application. In: Yonazi, J.J., Sedoyeka, E., Ariwa, E., El-Qawasmeh, E. (eds.) ICeND 2011. CCIS, vol. 171, pp. 223–237. Springer, Heidelberg (2011)
18. Kubicek, J., Penhaker, M., Feltl, D., Cvek, J.: Guidelines for modelling BED in simultaneous radiotherapy of two volumes: Tpv1 and Tpv2, 131–135 (2013). doi:10.1109/SAMI.2013.6480960
19. Pustkova, R., Kutalek, F., Penhaker, M., Novak, V.: Measurement and calculation of cerebrospinal fluid in proportion to the skull, 95–99 (2010)