

# Optical Digital Biopsy: Uveal Choroidal Melanoma: Case Report and Update of Technology

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## Abstract

*Introduction:* We report our initial observations on the technique of “optical digital biopsy” and its applications in a variety of diseases involving the vitreous, retina, retinal pigment epithelium, and choroid. In this case we present a patient with a diagnosis of intraocular choroidal tumors in which was replicated the optical digital biopsy with optimal results in our conclusions, confirmed later by enucleation. Optical Digital Biopsy is a noninvasive technique that allows the assessment of cellular composition and tissue, but the refinement of technique and additional validation studies are still necessary before being able to apply it clinically. This report includes an update of the technique and its possibilities.

## Keywords

Optical Digital Biopsy, Intraocular Choroidal Tumors, Update

## 1. Background

“Optical Digital Biopsy” comprises of two essential components: firstly to capture a high resolution in vivo digital image and then secondly, to unmask the digital image by post processing means so as to achieve tissue and cell identification. In Optical Coherence Tomography is possible to capture retinal images 40 to 50 times faster and with higher resolution (axial resolution of less than 4 microns) than standard time domain with optical coherence tomography.

We report our initial observations on the technique of “optical digital biopsy” and its applications in a variety of diseases involving the vitreous, retina, retinal pigment epithelium, and choroid. In this case we presented a patient with a diagnosis of intraocular choroidal tumors, in which was replicated the optical digital biopsy, with optimal results in our conclusions, confirmed posterior, through the enucleation.

## 2. Material and Methods

Review Board approval was obtained (MU #). A male

patient, 58 years old, refers a pain, with a fast and progressive loss of vision. The end ophthalmic diagnosis was based on clinical history, ophthalmoscopic examination, angiographic studies, ultrasonography and biopsy (FNBP). Optical Coherence Tomography (3D OCT-1000, Topcon Inc., Paramus, NJ) was used in this study. The axial resolution of this OCT is between 5-6 microns with the data-acquisition speed of 18,000 scans/second. For the study, patients were imaged using a “3D-scan program” with macular fixation (127 B-scans covering a retinal area of 6.0 x 6.0 mm).

The digital processing of the spectral domain optical coherence tomography images was performed by using standardized multiple sequential steps categorized into 3 basic algorithms based upon presumptive clinical diagnosis: degenerative lesion (I), neoplastic lesion (II), and vascular lesions (III). Those automatic settings exist within the commercially available imaging programs that are essential to keep images, as pure as possible, but may be altered to enhanced cellular morphology by overcoming pixelation to obtain cell bound.

### 3. Results

The results of this work are necessary make difference in many steps related to the progressive transformation of an

optical coherence tomography image in microscopical changed. The effect actually is exclusively digital. (Figures 1, 2, 3 and 4.)

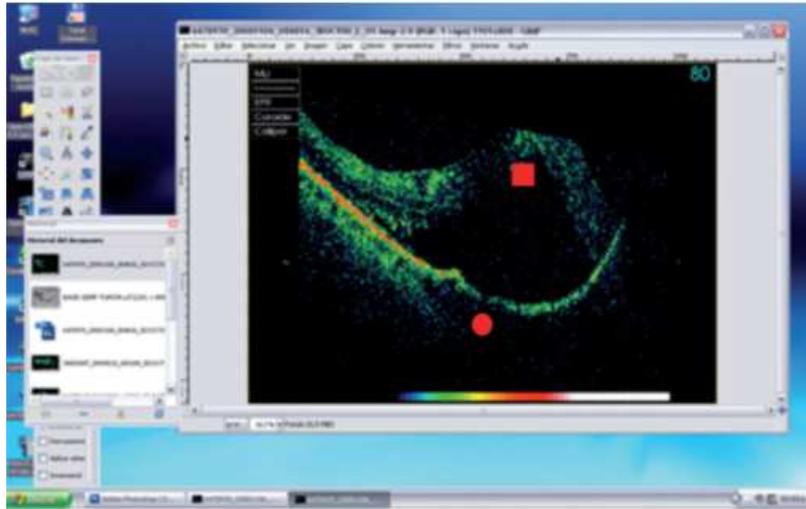


Figure 1. Optical coherence tomography: retinal detachment with Bruch rupture

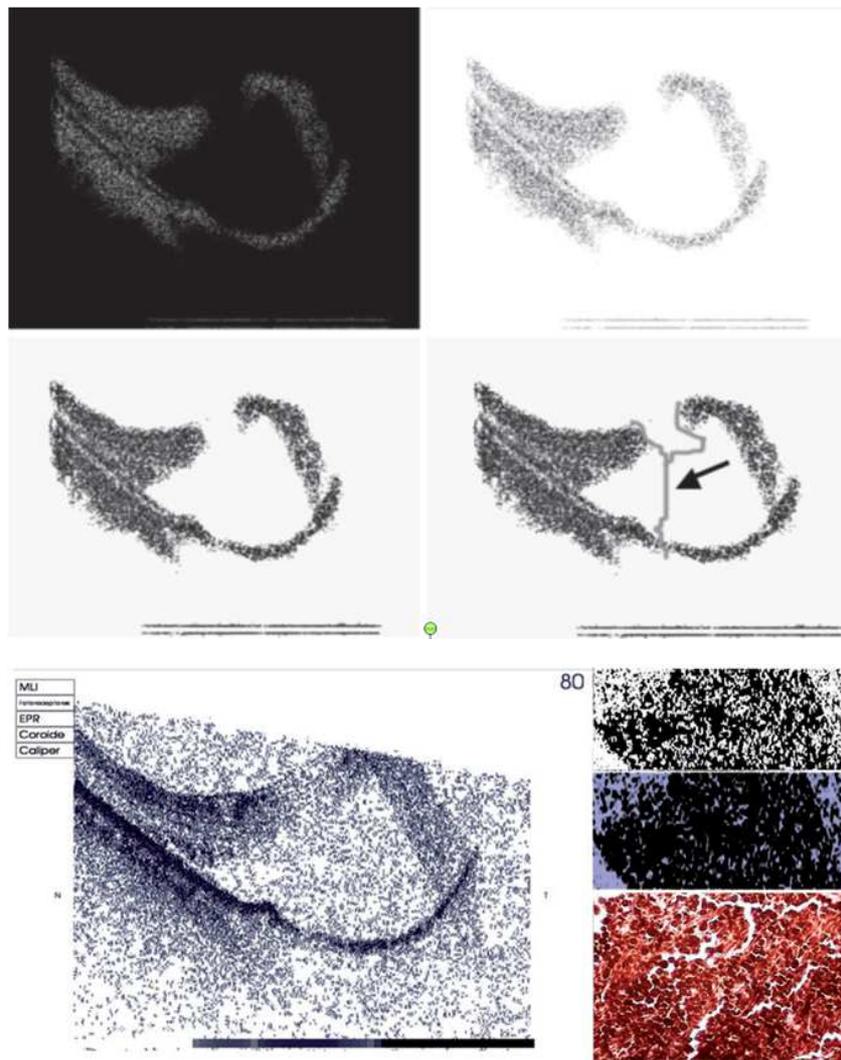
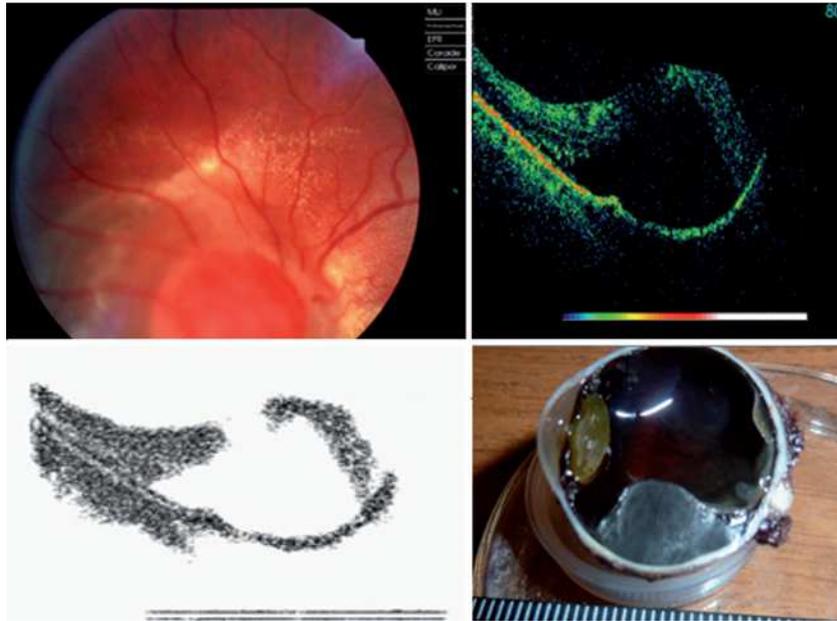
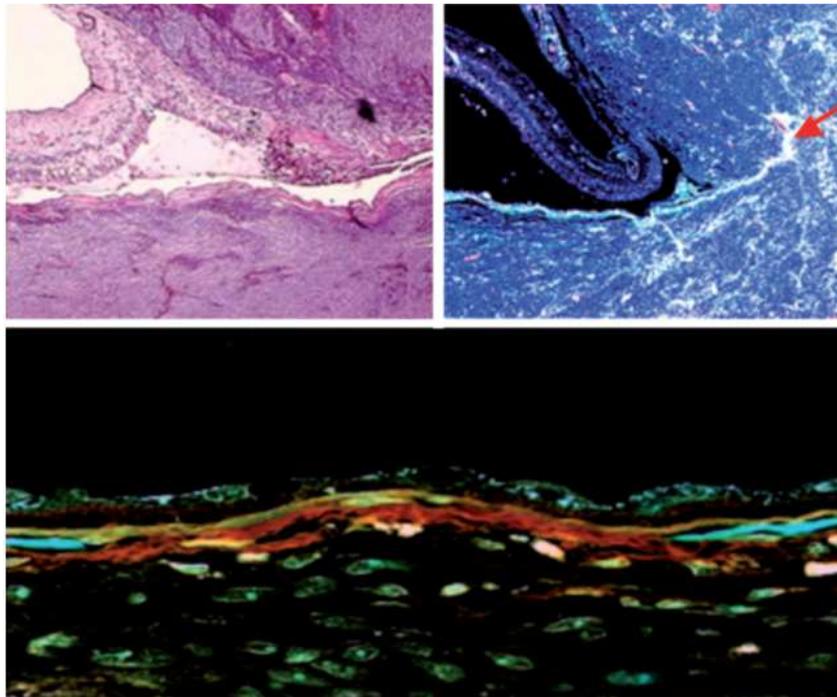


Figure 2. Subtraction of nodular image. We can observe the rupture of internal part of retina and vitreous invasion. Left, image of retinal detachment. Right, three successive imagines of steps in the processing



**Figure 3.** Resume of the case. Fundus, Optical coherence tomography, Step of optical digital biopsy .Enucleation. Correlation of the different image.



**Figures 4.** Histopathological cuts of this case post enucleation. The structure repeats observations with the optical digital biopsy technique. Arrow: Edge rupture of Bruch membrane, by tumor's infiltration

#### 4. Discussion, Update and Future Research

The digital optical biopsy is a process that we are studying for more than 5 years, in order to transform images from optical coherence tomography (OCT) to a preparation of microscopic histological and cytological nature. The results obtained so far are encouraging, still in the beginning stage in a structuring software, essential element to replace the more than 40 steps we do at present (time factor), and

methodological reproducibility (precision factor) .

The basis of this method is to accept the hypothesis that supports the pixels as binary image units, taking into consideration their different types (shape, clustering, etc.) Which are arranged as a genome like, giving the tissue specificity expressed.

We think that the same procedure can be used on the basis of complementary imaging studies (ultrasound, resonances, video endoscopy, etc.), with other tissues of other organs and systems. Neither microscopes nor tissue processing, seem essential to diagnose an injury, in those areas where the

digital image capture is implemented to study.

Part of the methodology, based primarily on the pixelography and pixelometry, taken as a form of geometry, ranging from scheduled acquisition and sharing of digital images, neatly arranged in the areas of material to study. Determination of the values of the pixels, and processing in all its measurable skills, both metric and geometric. Processing and reconstruction of new features in the image, with pulse sequences and levels of inference.

Mutual information with multimodal histograms results and estimate deviations and errors.

Comprehensive use of data stored in a digital image based on the concept on the integration of the time factor in it. Every digital image has inside, apart from their resolving power, an information that integrates it in milliseconds different morphological cuts. Its maximum capacity for information and detecting are in the pixels that configures it, able to be used by tools smart enough to remove it.

These considerations led to the practice of many examples in the study of the morphology of the retina (in our case), allow us to infer that analogous or with similar sequences of energy can be obtained histological images of different tissue as noninvasive biopsies.

The basis of the method is combined basis in spectrometry and interferometry, optical analysis, application of light amplification stimulated emission radiation (laser). All the laws of quantum physics, and basic fundamentals of coherent light are applied. Both temporal and spatial coherence. The system relies on the absorption or transmission of the radiation by a solute  $x$ ; in turn is considered as Beer's law concentration  $x$ , and according to the law of Lambert or Bougert -Beer -Lambert distance of the emitted light and the solute  $x$ . The image segmentation cell and tissue was performed using the image processor. In the images of isolated cells, we can see three areas: the nucleus, cytoplasm and background. In the cohesive tissue images are even more irregular. In all cases, the most important thing is to determine the total number of pixels in the image, they

contained within the cytoplasmic membrane, the number of pixels contained in the nucleus, cytoplasm and proportions by area and size.

This procedure is intended to align the image for further analysis, performing, and band extraction, image smoothing and extracting the region of interest, which converts an image in a binary image. Then soften the image containing the image detail, since it acts as noise for the purpose, which is the region of interest containing pixels to represent optimally. Proper selection of the region of interest can operate only on the pixels that contain relevant information. That's why obtaining the required parameters for treatment and any work on the image conversion is done by segmenting, thresholding from information provided by the histograms of the gray levels of the processed images and the corresponding averages.

The methodology is repeatedly pixelométric, pixelográfica and could add pixeloarchitectural. Each binary image, which led to the subcellular level could be a protein has a code based on pixels, with many likely exceeding the genome.

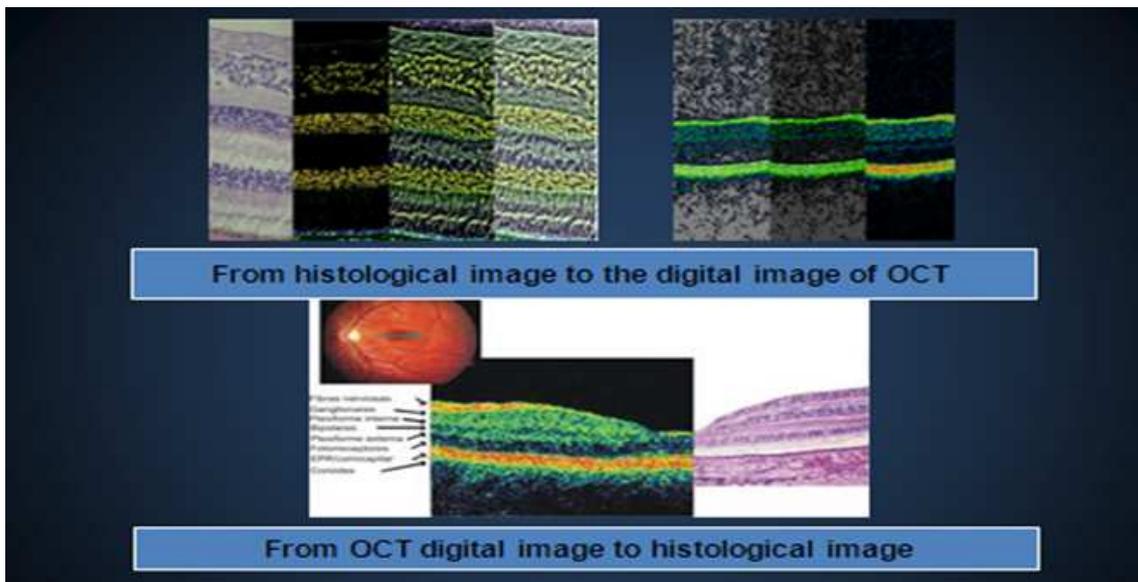
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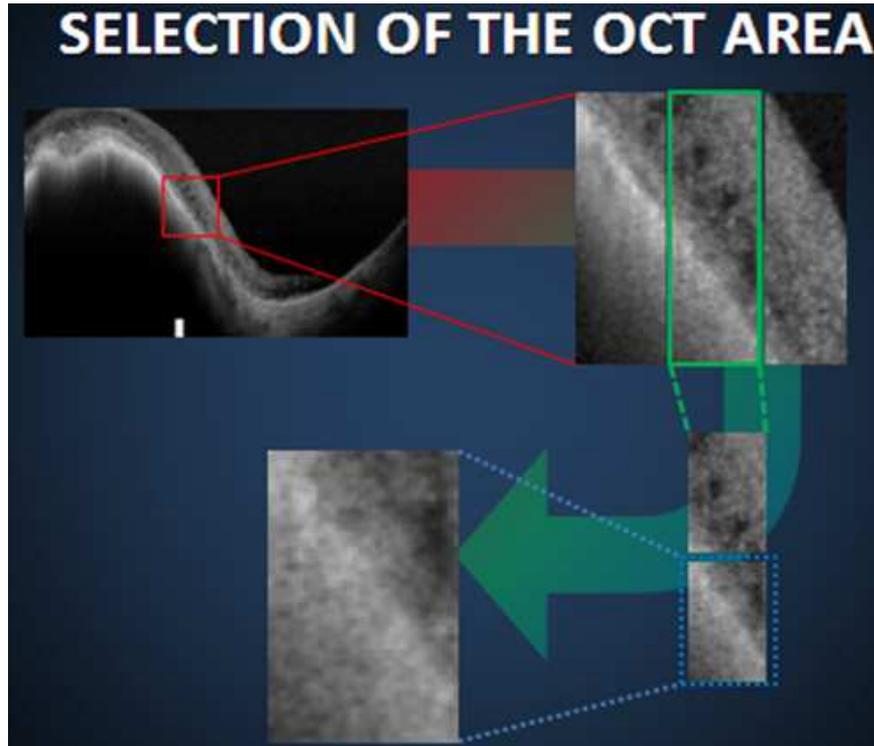
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- application of light amplification stimulated emission radiation (laser).

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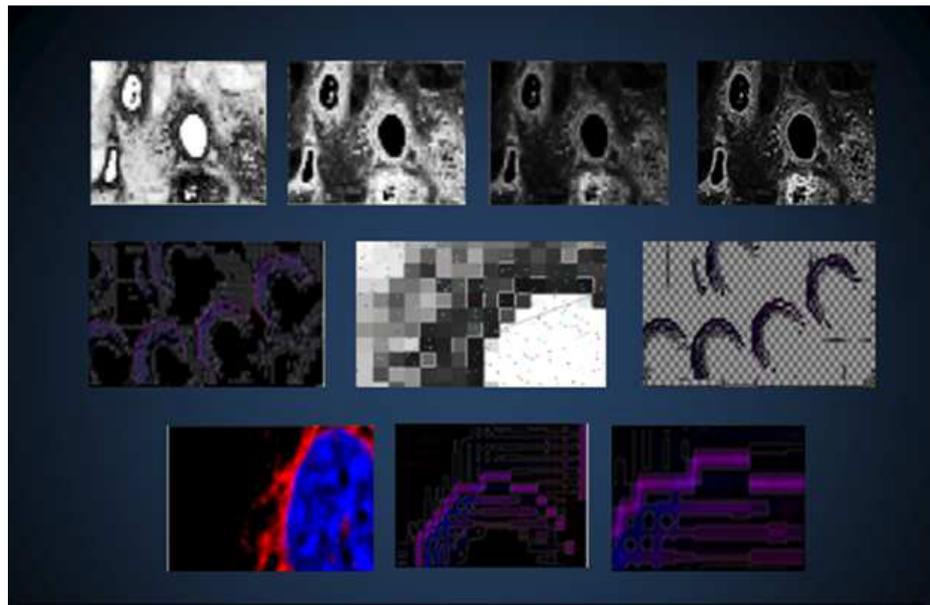
Swept source OCT allows observed choroidal substructures. The possibility of obtain a histological image from an image obtained by OCT is possible, the steps of the transformation are based on what we called "pixelometric" and "pixel architecture" laws. Digital Biopsy (Figure 5, 6)

BOD©CCF-019620 us-pat. Futures studies allow to evaluate these new technologies.





**Figures 5.** The method are resume in the first image. Microscopy to OCT, and them OCT microscopy source.



**Figure 6.** Pixelometric steps, with tonal curve, bordes, etc to the cell image

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