Journal of Medical Hypotheses and Ideas (2015) 9, S14–S23

Available online at www.sciencedirect.com

Journal of Medical Hypotheses and Ideas

journal homepage: www.elsevier.com/locate/jmhi

REGULAR ARTICLE

Towards a histological depiction in 3D imaging PET

Marios Poulos [a,*], Theodoros Felekis [a], Angeliki Poulou [b]

[a] *Laboratory of Information Technologies, Ionian University, Greece*
[b] *Department of Materials Science and Engineering, University of Ioannina, Greece*

Received 9 September 2015; revised 21 January 2016; accepted 21 January 2016
Available online 8 February 2016

KEYWORDS

VEGF;
PET;
RBF neural network;
Simplified reference tissue model;
BP

Abstract In this study we examine the possibility of constructing metadata from Positron Emission Tomography images based on a Radial Basis Function neural network, which uses histological data extracted via the enzyme-linked immunosorbent assay abbreviation. The aim of constructing such metadata is to achieve a bringing between the binding potential receptor *in vitro* and *in vivo* Positron Emission Tomography procedures, which it is possible to calculate using a classic simplified reference tissue model. This knowledge representation procedure may then be transmitted in the Positron Emission Tomography using the testing neural network procedure. The latest satisfies the primary aim of this study, which was to avoid painful and risky biopsies of patients.

Introduction

Biopsy for histological assessment is an important tool in the diagnosis and management of cancer. This traditional method helps resolve and characterize the stage of the disease by giving a straight therapeutic line in patients with tumor tissue. But this method also has a low possibility of seeding tumor cells. Indeed, research suggests that after diagnostic biopsies of tumors, many patients developed cancer [1].

Numerous clinical studies have related the connection between tumor tissue and angiogenesis. Meanwhile, there is a correlation between an increased number of new vessels and the progress of metastasis. Recently, researchers have extensively studied this mechanism, because it is widely believed that pre-cancerous tissues acquire angiogenic capacities on their way to becoming dangerous. Among various regulators of angiogenesis, researchers believe that a vascular endothelial growth factor (VEGF) plays a pivotal role in augmenting all steps of angiogenesis [2,3].

* Corresponding author. Tel.: +30 2661087429; fax: +30 2661087433.
E-mail address: mpoulos@ionio.gr (M. Poulos).

URL: www.tums.ac.ir/english/
doi:http://dx.doi.org/10.1016/j.jmhi.2016.01.001

The abnormally fast growth and division of tumors drives the overexpression of the VEGF. The VEGF supplies more oxygen and nutrients, which results in dramatic changes in the molecular mechanism of cancer. At this point, VEGF discrimination and detection in blood in low concentrations could be a high-priority research parameter, which would create an innovative tool in the field of data mining systems; this topic has not been explored [1]. One popular method of assaying VEGF is the enzyme-linked immunosorbent assay (ELISA). ELISA is a popular "wet-lab"-type analytic biochemistry assay that uses a solid-phase enzyme immunoassay (EIA) to detect the presence of a substance, usually an antigen, in a liquid sample or wet sample [2]. VEGF is an antigen consisting of dimeric glycoproteine, which consists of a significant parameter during physiological and pathological angiogenesis [3].

It induces germinating angiogenesis, improves vessel permeability, and controls vasculature restructuring and several pathologies [4,5]. It is produced in arteries, veins, and lymphatic tissues, where its role is to restore oxygen supply to tissues when blood circulation is inadequate. Hypoxia stimulates the expression of the VEGF protein [6–9].

The overexpression of VEGF is an index for cell abnormalities, diseases, and several intraocular symptoms. *In vitro* studies have shown that pathological angiogenesis [6,7] and neovascular disorders cause the growth and migration of cells [10,11]. An increased concentration of VEGF is correlated with poor patient survival, reduced cell function, and early-stage metastasis. Thus, this dimeric protein provides a useful marker and is a measurable element of tumor biology.

Only a few studies treat the quantification of the VEGF protein, but ELISA forms the basis of one of the most common techniques used in this type of research [4,12,13]. Studies have shown that the quantification of VEGF and other angiogenic peptides in tissue, together with measurement of neovascularization in the tumor itself, may be used to increase the accuracy of prognosis for patients with brain tumors [4]. The concentration of VEGF in healthy and brain-cancer patients was observed by directly measuring VEGF using ELISA. This research revealed significantly elevated levels in the tissue and cyst fluid of glioblastomas, suggesting that VEGF is a measurable parameter of brain tumor biology [4].

The *in vivo* procedure, Positron Emission Tomography (PET), is a very sensitive quantitative method used to describe tissue penetration. PET has been widely used in clinical oncology for tumor staging and for measuring tumor glucose metabolism. PET indirectly measures VEGF by using the concentrations of tracers such as an 89Zr-labeled tracer [14]. Fig. 1 depicts the usual procedure for verifying a cancer diagnosis via clinical routines and research studies.

The clinical routine is divided into two procedures: *in vivo* (MRI and PET scans) and *in vitro* (biopsy and histological assessment) procedures. The penultimate procedure consists of correlating the imaging and histology assessments. Some questions that naturally arise from this procedure are: Is it possible to avoid the painful and risky biopsies as well as histological assessments? In recent years, several studies determined that the precision of the diagnosis analysis of various applied data mining classification techniques, as well as the execution of those techniques, are acceptable to support medical professionals in making primary diagnoses and avoiding biopsies [4]. Is there any reason the data extracted from histological examinations conducted on some patients could not be applied to other patients? Is it possible to use data mining to extract information from biopsies and histological assessments, and to use these data in conjunction with MRI and PET images? The present study answers these questions.

In artificial intelligence science, artificial neural networks (ANNs) consist of a category of statistical learning model that is based on biological neurons. ANNs train and obtain knowledge from standard data. The training procedure of ANNs successfully simulates the functionality of a small biological neural cluster. Nowadays, medical professionals in several disciplines apply ANNs for medical diagnosis. The structure of these networks consists of hidden notes and weights that connect the neurons with different types of logic. Thus, there are several types of ANNs: networks that contain Radial Basis Function

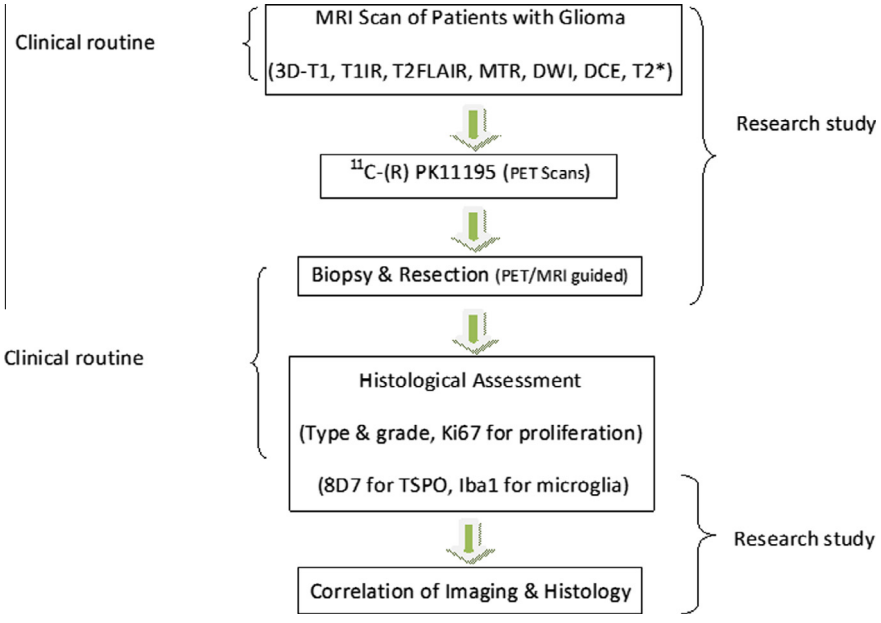

Figure 1 A typical series of clinical routines and research studies used in cancer diagnosis.