



Determination of Chronic Disease Origin Using Time Reversal Computations

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Abstract

All chronic inflammatory processes in a living organism pass through a series of biological stages to form tumors. This is similar to a natural effort to repair a chronic wound. Sometimes, the origin of metastasized tumors cannot be located with our conventional biomedical and biochemical tools. However, each tumor has a specific growth rate based on an individual's health status. The tumor growth rate can be calculated from the CT scan information taken at different time intervals. Then one can determine the tumor's initiation time at cellular level with the help of growth rate parameters. A time reversal mathematical model has been proposed to determine the initiation time of a tumor. This model can be used to estimate the origin of some tumors for better treatment planning in chronic diseases. Since cancer is not a local malady the holistic approach is required to analyze the possible root cause of this degenerative disease.

Keywords: Chronic; Diseases; cancer; CT

Background Introduction

Studies indicate that about 45% Americans entered the 21st century carrying chronic diseases with them. About 61 million among these patients had multiple chronic conditions [1]. The chronic diseases consume 78% of the health spending budget in the USA. The majority of victims suffering from chronic diseases fall in the age group of 65 and older.

It has also been reported that 85% of our seniors are suffering from chronic diseases while 62% have multiple chronic conditions.

Female patients have more chronic conditions than male population. About 46% white and 37% black have reported chronic conditions in some research studies. But the chronic conditions almost equally affect different income classes across the board (41% poor, 46% near poor, 44% low income, 43% middle income, and 44% high income). According to another, study the cost of chronic diseases amounted to \$277 billion in the USA during 2003 fiscal year. The lost in productivity due to chronic diseases during the same period reached one trillion dollars. The news about chronic diseases at global level is also alarming. According to the World Health Organization (WHO) report, 59% of deaths and 46% of the global burden of diseases are attributed to chronic maladies [2]. The lack of resources, infrastructure and know-how of conventional therapies make it impossible to deliver meaningful health benefits to a great majority of patients in the developing world [3-5]. As most of the populace resides in the countryside, any conventional medical facility is mostly inaccessible to them anyway. There is an urgent need to explore alternative methods to combat chronic diseases at an early stage throughout the world [6].

Historically homeopathy has prided itself in dealing with the chronic diseases since its early days. The epitome of chronic diseases philosophy in homeopathy was authored by Hahnemann himself almost two hundred years ago [7]. While dealing with chronic diseases, he was forced to challenge some of his own earlier theses about medicine. Hahnemann's dramatic departure from classical homeopathic philosophy was primarily because of the complex nature of chronic diseases. First, he introduced the name "disease" as the title of his new book "Chronic Diseases". But in his earlier philosophy of similia, he vehemently rejected to label any sickness with the word disease [8]. Second, he coined the term "anti" i.e., anti-miasmatic, anti psoric, etc. This was in direct contradiction with his original philosophy

of "homeo", the hallmark of his new system of medicine popularly known as homeopathy. Third, Hahnemann advocated the alternation of medicines in stubborn chronic cases. But he strictly accentuated about single remedy in his prior philosophy in the "Organon of Medicine". Fourth, the strengths of drugs were also revised though he claimed that drugs get highly energetic with his regular centesimal succession. Fifth, the dominant factor in chronic diseases was miasma. The vital force was not any more the sole contender in guaranteeing health. The role of miasma can be elucidated from the fact that Hahnemann mentioned it about one hundred times in his book Chronic Diseases. The word vital force is barely mentioned about a dozen times in the same manuscript. The word vital force is mentioned over 200 times and miasma about 50 times in the Organon of Medicine. In nutshell, the nature of chronic diseases even forced Hahnemann to abandon his original philosophy and venture on to a different course. This also shows the level of complications embedded in chronic diseases and the time required in setting back the convoluted biological evolutionary processes to their original course. Unfortunately, there were no serious efforts after Hahnemann to address the nature of chronic diseases in depth on scientific lines [9].

Cancer is mostly referred as an ulcer in Hahnemann's works. Today, cancer is considered as the most deadly disease among chronic maladies. It formed merely 3% of the total disease burden at the turn of the last century. Just in one hundred years cancer has affected almost 45% of the patients in the United States alone. Subclinical chronic inflammations, mostly from suppressed diseases, eventually lead to tumor formations. Organs consisting on parallel sub functional units, such as liver, lung and kidneys may breed tumors for years without any observable signs or symptoms. Cancerous cells from these sites

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dislodge and migrate through circulatory systems to distant parts of the body. For instance tumors found in brain mostly originate in lung [10]. The chemotherapy is limited in treating brain tumors because of the limitations of blood-brain barrier. Brain tumors are mostly treated with radiation and surgical techniques for local control. The combined applications of these marvelous clinical techniques could not extend the survival time beyond one year [11].

Even with combined whole brain radiation therapy and stereotactic radiosurgery (SRS), the median survival rate was only 11 months [12]. Survival rate for patients suffering from brain cancers is much better than patients suffering from brain tumors [13-17]. It has been reported that when the cancer origin was liver, the poor patients had not even time to get treated as their conditions deteriorated quickly [18]. There is also a tumor spread from Non-Small Cell Lung Cancer (NSCLC) to other organs such as lymph nodes, pleura, brain, liver, bone, pericardium, and renal system [19]. Furthermore, there can also be some rare cases when tumor spread to brain occurs from endometrial carcinomas [20]. The prominent cancer that spreads to other organs originates in lung [21]. Intracranial metastases are mostly from lung, breast, renal and skin i.e., melanoma origin. It has also been found that about 70% intracranial lesions are located within the brain parenchyma, the rest involves the pachymeningeal envelopes. Intracranial metastasis makes up to 17% of all brain tumors [22]. However, only 15% patients die due to brain metastasis [23]. Leptomeningeal metastases have origins in leukemia, lymphoma and breast carcinoma but these are rare. Computed Tomography (CT) scanning is state of the art technology to acquire appropriate information about site, size, and morphological metastasis of the brain tumors.

It has been suggested that a holistic approach, in addition to local treatment, may well enhance the quality and length of lives for cancer patients [24]. Such a treatment plan needs comprehensive information about a cancer patient. Since cancer masks the most of the conventional symptoms, there is a need to plan an elaborate strategy to evaluate cancer as a chronic disease. For instance, researchers have found that they could not find significant differences in tumor distribution between symptomatic and asymptomatic patients in non-small cell lung cancer with brain metastasis [25]. An alternative solution to this problem is to trace out the possible root of a tumor. A mathematical model has been developed to estimate the possible initiation time of a tumor. A physician can use this model to investigate the patient's medical history.

Materials and Methods

Different models have been in use to estimate the tumor growth rate [26,27]. Meanwhile different techniques have also emerged to utilize Computed Tomography (CT) information to determine tumor volume [28]. These volume growth rates can be generalized for particular kind of tumors as it varies from patient to patient [29-30]. Some otherwise healthy individuals may have very slow growing tumor while patients suffering with multiple chronic diseases have accelerated growth rate. It is possible to determine growth rate for an individual based on tumor volume at two different points of time. The following model can be used to individualized patients when two different scans are compared over time. Mühe et. al. have reported that among different patients, the doubling time varied as between 50 days and 860 days in squamous cell carcinoma's, 22 day to 2098 days among soft tissue sarcoma, 15 days to 2798 days among sarcoma of bone etc. [31]. So the case of chronic diseases is highly individualized among patient though suffering from the same type of cancer. Hence, an approach based on individual patient is required to analyze the case in a holistic manner.

Estimating the roots of chronic diseases

Change in tumor volume, V, with time can be defined as,

$$\frac{dV}{dt} = \eta V$$

Where η is growth rate constant for a particular tumor.

$$\frac{dV}{V} = \eta dt \tag{A}$$

Suppose the initial volume of tumor is V_1 at time t_1 and as tumor grows its volume at time t_2 reaches V_2 . Integrating equation (A)

$$\int_{V_1}^{V_2} \frac{dV}{V} = \eta \int_{t_1}^{t_2} dt$$

$$\ln\left(\frac{V_2}{V_1}\right) = \eta(t_2 - t_1) = \eta \Delta t \tag{B}$$

Taking exponential on both sides

$$V_2 = V_1 e^{\eta(t_2 - t_1)} = V_1 e^{\eta \Delta t} \tag{C}$$

Equation (B) can also be rearranged as,

$$\eta = \frac{\ln\left(\frac{V_2}{V_1}\right)}{(t_2 - t_1)} \tag{D}$$

Or

$$\Delta t = (t_2 - t_1) = \frac{\ln\left(\frac{V_2}{V_1}\right)}{\eta} \tag{E}$$

Suppose $\Delta t = \tau$ is the time when tumor volume doubles from volume V_1 to V_2 i.e. ($V_2 = 2V_1$), then we have from equation (E)

$$\tau = \frac{\ln(2)}{\eta} \quad \text{Or} \quad \eta = \frac{0.693}{\tau}$$

Using the value of η in equation (D) and after rearrangement

$$\tau = \frac{0.693(t_2 - t_1)}{\ln\left(\frac{V_2}{V_1}\right)} = \frac{0.693t}{\ln\left(\frac{V_2}{V_1}\right)} \tag{F}$$

Or

$$V_2 = V_1 e^{\frac{0.693(t_2 - t_1)}{\tau}} = V_1 e^{\frac{0.693t}{\tau}}$$

$$\ln\left(\frac{V_2}{V_1}\right) = \frac{0.693(t_2 - t_1)}{\tau} = \frac{0.693t}{\tau} \tag{G}$$

Example 1

If the initial volume of a tumor was measured to be 1.23 cm³ and after 14 months, the tumor size is 1.45 cm³. What would be the doubling time τ for this tumor?

Solution: using equation (F) we can estimate the doubling time

$$\tau = \frac{0.693 \times 14}{\ln\left(\frac{1.45}{1.23}\right)} = \frac{9.702}{0.16455} = 58.96 \text{ Months}$$

So from above calculation we figure out the doubling rate of this tumor is ~ 59 months, which is almost 5 years. This is an example of very slow growing tumor, such as Prostate.

Example 2

Using images as shown in figure 1A and 1B, if the tumor growth rate is $\tau = 5 \text{ months}$ and the current volume measured through CT scan is $\sim 3 \text{ mm}^3$. Suppose the volume of single cell for such cancer is $10 \mu\text{m}^3$ when the initial cancer started?

Solution: using equation (F)

The radius of tumor cell, $r = 5 \mu\text{m}$

The volume $V_1 = \frac{4}{3}\pi r^3 = 5.236 \times 10^{-16} \text{ m}^3$.

$$\tau = \frac{0.693 \times t}{\text{Ln}\left(\frac{V_2}{V_1}\right)}$$

After rearrangement

$$t = \frac{\tau \times \text{Ln}\left(\frac{V_2}{V_1}\right)}{0.693}$$

$$t = \frac{5 \times \text{Ln}\left(\frac{3 \times 10^{-9}}{5.24 \times 10^{-16}}\right)}{0.693} = \frac{5 \times 15.56}{0.693}$$

$t = 112.3 \text{ Months}$ or over 9 years.

Check with the patient what happened 9 years ago in his/her medical history tries to locate the root of diseases in that region

Conclusion and Discussion

The use of toxic drugs, continuous exposure to environmental particulates, inhibitions of evolutionary biological processes, suppressions of infectious diseases and administration of hormones form the root causes of chronic maladies. These prolonged external assaults initiate necrotic foci in the biological systems. Most of these necrotic centers release chemical signals during subsequent repair processes. In reaction the affected system produces localized

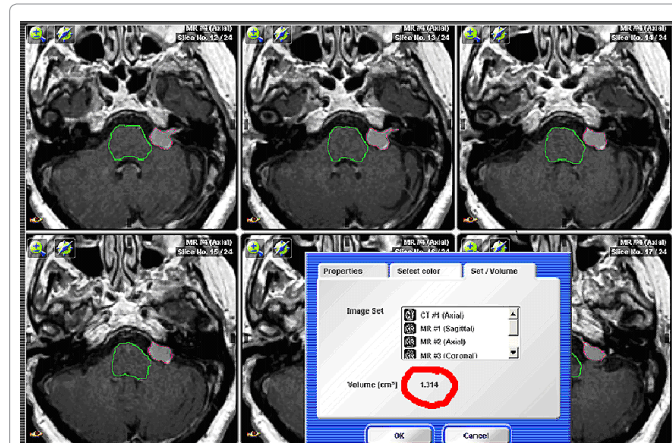


Figure 1b: Tumor volume after 5 months.

inflammation. Such inflammatory processes resemble chronic wounds that never heal. Using the above information a physician can explore the medical history of the patient. In the above case, the physician can inquire what happened 9 years ago. Since most cancers arise from chronic diseases, it would be prudent to heal the system at the root level. Almost all the local controls in cancers are limited and patients die soon after they are treated. It will be advisable for patients to have alternative therapy for chronic conditions along with conventional medicine. Caution must be observed that all tumors do not grow exponentially. It is true especially with breast/prostate tumors and in laboratory animals where the subject is otherwise healthy. However, tumors involving the deterioration of the entire system grow exponentially. Again one must keep in mind that estimating tumor volume is subjective and two experts may not agree or even one expert at two different occasions may come up with different results. Automated computer based imaging tools may be more reliable in assessing the tumor volume.

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Conflict of Interest

No financial involvement with any person or organization is related to this study.

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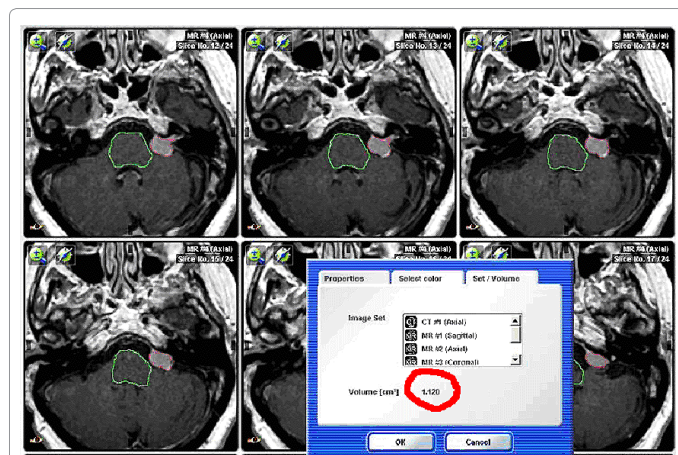


Figure 1a: The contouring of Acoustic Neuroma of the right side of a patient. The tumor volumes are computed by the software. This is a teaching example and may not be clinically valid.

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