

# The Genetic Reversibility in Oncology

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## ABSTRACT

With the aid of an original semeiotics' method we investigate the different stages of the process of Oncogenesis, according with 'Quantum Biophysical Semeiotics' priors, to reveal the presence of 'Oncological Terrain' and 'Inherited Real Risk' of cancer. Thos diagnosis allows a primary and pre-primary prevention with recursive effects able to reverse the genetic alteration of mit-DNA and the mitochondrial cytopathy at the base also of Oncological pathologies.

## Introduction

This paper highlights the central role of mitochondria and mitochondrial DNA (mit-DNA) in the process that underlies the transformation of a healthy cell into a cancer cell. For this purpose is essential the knowledge of 'Quantum Biophysical Semeiotics', QBS, extension of the medical semeiotics with the support of quantum and complexity theories, a scientific approach based on the 'Congenital Acidotic Enzyme-Metabolic Histangiopathy', CAEMH [1], a unique mitochondrial cytopathy, present at birth and subject to medical therapy.

According to Stagnaro's works, the doctor can bed-side evaluate, simply using the stethoscope [2], the mitochondrial functionality of the patients in all biological systems. It is possible, since birth, to make a diagnosis in order to detect the presence of 'Inherited Real Risk' of cancer linked to a specific 'QBS Constitution', i.e., 'Oncological Terrain' [3], so that an intelligent prevention in subjects with 'Inherited Real Risk' [4] can be implemented. On the basis of 'QBS Constitutions' [5] - i.e. 'Hypertensive Constitution', 'Diabetics Constitution', and so on – it can be prevented the onset of more serious diseases such as, i.e., cancer, diabetes, ischemic heart diseases, including myocardial infarction.

Finally, QBS has been related to the 'Principle of Recursive Fractal Genome Function' (PRFGF) introduced by Pellionisz [6], corroborated from the clinical QBS view-point [7], in order to understand if the genetic alteration of mit- DNA can be reversed, due to the recursive energy, information and communication feedback between DNA, RNA and downstream structures such as tissues, cells, mitochondria and proteins.

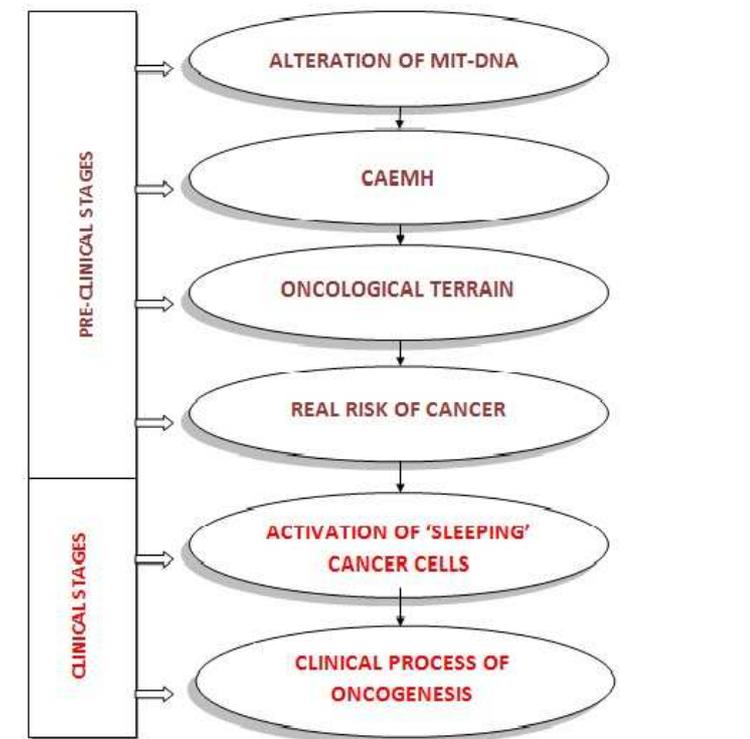
First of all, in chapter 1 the process of Oncogenesis according with QBS is evidenced. Secondly, in chapter 2 some elements of QBS method for the diagnosis of 'Oncological Terrain' and 'Inherited Real Risk' of cancer are shown. Finally, the chapter 3 is dedicated to QBS primary

and pre-primary prevention, evidencing the genetic and no genetic effects of different kind of therapies.

### 1. The process of Oncogenesis: 'Oncological Terrain' and 'Inherited Real Risk' of cancer

According to Stagnaro [8], genoma's information are transmitted simultaneously both to parenchyma and related microvessels, so that mutations in parenchymal cell n-DNA and mit-DNA are the *the conditio sine qua non* of the most common human disorders, like diabetes and cancer, today's growing epidemics. In fact, all these diseases are based on a particular congenital, functional, mitochondrial cytopathy, mostly transmitted through mother, and defined 'Congenital Acidotic Enzyme-Metabolic Histangiopathy', CAEMH [9].

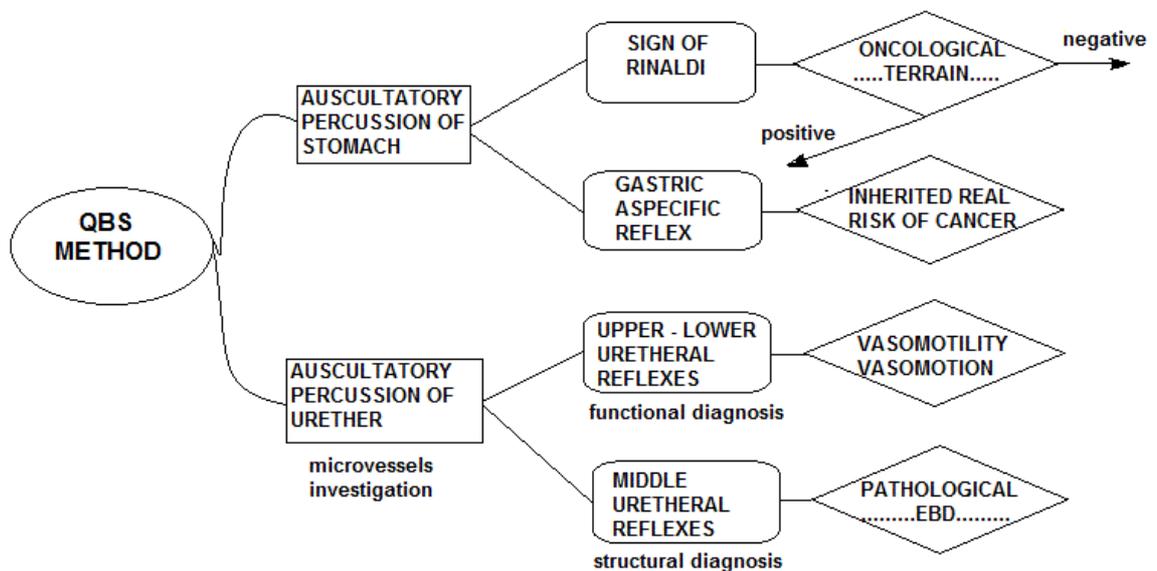
In addition, parenchymal gene mutations cause local microcirculatory remodeling, gathering indirect information on inherited modifications of relative parenchymal cell, since biological system functional modifications parallel gene mutation, according to Angiobiopathy theory [10]. The presence of intense CAEMH – termed CAEMH- $\alpha$  - in a well-defined myocardial area, involved by gene mutations in both n-DNA and mit-DNA, is the ground for the 'Oncological Terrain', one of the 'QBS Constitutions' which could bring about the congenital Real Risk - RR<sup>ii</sup> of cancer (Scheme 1) characterized by microcirculatory remodeling, from QBS view-point, intense under environmental risk factors.



Scheme 1. The process of Oncogenesis

## 2. QBS diagnosis of Oncological Terrain and Inherited Real Risk of cancer

By means of the QBS the doctors are able to evaluate the pre-clinical stages of the process of Oncogenesis of their patients, as shown in Scheme1, so it is possible a pre-clinical diagnosis of the potential pathology, at bed-side, before the clinical diagnosis<sup>iii</sup>, i.e., the activation of 'sleeping' cancer cells [3, 8], which start the clinical process of Oncogenesis. The objective QBS examination allows, in a few minutes, to recognize and quantify, in a subject, the presence of CAEMH, 'Oncological Terrain' and 'Inherited Real Risk' of cancer (Scheme 2), i.e., evoking 'Gastric Aspecific Reflexes' through the 'Auscultatory Percussion' of the stomach [2]. Furthermore, the diagnosis can be refined through microvessels investigation, evoking 'Ureteral Reflexes' from a functional point of view, i.e., vasomotility and vasomotion [Appendix A] , and by means of a structural examination, i.e., by the observation of EBD<sup>1</sup> - Endoarteriolar Blocking Devices within small arteries, by Hammersen [11] - , type I, subtype a) cancerogenous b) nonspecific (present in all the other more frequent and severe disease).



Scheme 2. Quantum Biophysical Semeiotics method based on Auscultatory Percussion of stomach and ureter

<sup>1</sup> The EBD is a kind of dam which opening or closing itself regulates blood flow in microvessels directed to the parenchyma (tissue, substance of a body). With a simple stethoscope it is detectable if there is a clear genetic predisposition to have a disease such as cancer or diabetes, and we can quantify and monitor it over time from birth. So there is the possibility of implementing a prevention on a huge scale in individuals clinically finally selected in a rational way. This new way to prevent illness will not allow to materialize the disease, but it can be anyway potentially present (or be RR as "residual") at potential level. As similarity we can think of butterfly valves that regulate the flow and mixture of air and gasoline in car engines, since the EBD are dams that are simply regulating blood flow to the parenchyma, precisely cells of various tissues. If these EBD are tough, rigid, inelastic, there is RR. There are EBDs Type I, located in small arteries and Type II located in the arterioles but only type II is ubiquitous (in the sense that it is observed everywhere, in all arteries). Even these physiological types get sick or old. However, the other types, pathological-neoformed, are expressions of the RR, of potential disease, they occlude more, but through therapy they can be transformed from the subtype a) tumoral, to subtype b) aspecific, and then in "physiological" type, decreasing gradually their amount.

## 2.1 ‘Auscultatory Percussion’ of the stomach and ‘Gastric Aspecific Reflex’

### a) Diagnosis of ‘Oncological Terrain’: Rinaldi’s Sign

Based on QBS principles [12], “intense” stimulation with digital pressure applied upon trigger point of SST-RH neuronal centre (Figure 1), or epiphysis skin projection area, increases ATP, originating the condition of simultaneous response in related remote biological system.

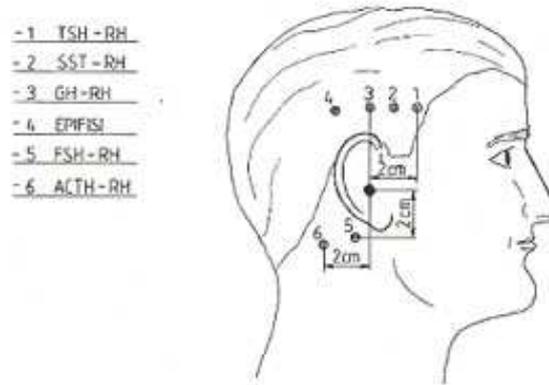
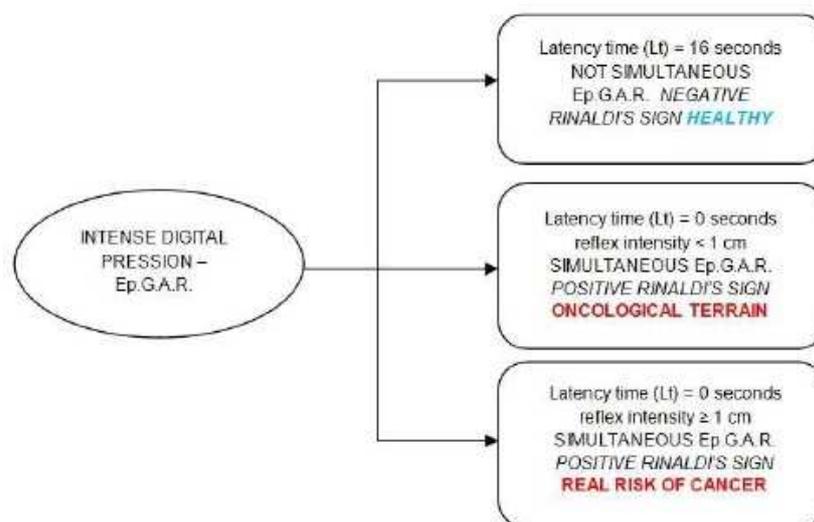


Figure 1

Under these conditions, in health, the reflex does not appear “simultaneously”, but after a ‘Latency time’ (Lt) of 16 seconds (Scheme 3): negative Rinaldi’s Sign, due to the associated stimulation of both parenchyma and related microvessel respiratory chain, providing adequate amount of ATP. In addition, the increased blood-flow remove  $H^+$  from the tissue, avoiding lowering pH. On the contrary, in individuals involved by ‘Di Bella’s Oncological Terrain’, we observe “simultaneously” the ‘Gastric Aspecific Reflex’ (Lt = 0) because the augmentation of tissue acidosis, since the impairment of microvessel reaction to stimulation: microcirculatory Oncological remodeling. The reflex’s intensity results less than 1 centimetre, paralleling the seriousness of underlying disorder: positive Rinaldi’s Sign. As a matter of fact, the intensity of the sign is directly related to the disease’s stage, so that it raises to about 3 cm. in overt cancer.



Scheme 3. Diagnosis of Oncological Terrain

## b) Diagnosis of Inherited Real Risk of cancer

If there is the 'Oncological Terrain' (positive Rinaldi's sign), we should refine the QBS diagnosis in order to understand at what stage the process of Oncogenesis is, i.e., if and where there is the 'Inherited Real Risk' of cancer. To this aim, the 'Gastric Aspecific Reflex', evoked under "mean" stimulation with digital pressure upon the trigger points of the related investigated parenchyma, plays a key role. For example, in Table 1, the liver 'Gastric Aspecific Reflex' (Li.G.A.R.), under light-moderate digital pressure on any point of the skin projection of the liver, is shown.

In health, the 'Latency time' of Li.G.A.R. is of 8 seconds while, in presence of 'Inherited Real Risk' of liver cancer in evolution, Lt is less than 8 seconds. We have to repeat the diagnosis after exactly 5 seconds from the first one (preconditioning), because in the beginning stages of 'Inherited Real Risk' of liver cancer, the Lt is still 8 seconds (the same of physiological one), but after preconditioning this value is less than 16 seconds (in health we observe exactly the double value).

Latency time (Lt) in seconds	Latency time after preconditioning (pause of 5 sec.)	Diagnosis
Lt = 8	Lt = 16	Health
Lt = 8	Lt < 16	Liver Cancer Inherited Real Risk
7 < Lt < 8	14 < Lt < 16	Liver Cancer Inherited Real Risk in evolution
Lt ≤ 7	Lt < 14	Overt Liver Cancer

Table 1. Liver - Gastric Aspecific Reflex (Li. G. A. R.)

## 2.2 Auscultatory Percussion and Ureteral Reflexes

The objective QBS examination of 'Gastric Aspecific Reflex' allows to recognize and quantify the presence of 'Oncological Terrain' and of the congenital 'Inherited Real Risk' of cancer, but the deeper investigation of microvessels and microcircle's function and structure is given by the 'Auscultatory Percussion' of ureteral reflexes.

Investigating the micro-vessels, whose behavior is that typical of dissipative systems far from equilibrium, this is a way to get indirect information from the state of health of their respective parenchyma. In case of an intense CAEMH, mitochondria and mitochondrial DNA (mit-

DNA) are genetic altered and play a central role in the process that underlies the transformation of a healthy cell into a cancer cell.

The Oncological Terrain (OT) as introduced by Stagnaro (2004) is instead expression of reduced defense (of gravity in growing) of the body mediated by PNEI system (Psycho-Neuro-Endocrine-Immunological system) in front of cell degeneration, and thus of the possible Oncogenesis, which occurs in every individual independently of the presence or absence of OT and of the gravity of the possible CAEMH. The OT is detectable at birth, because the intense CAEMH<sup>iv</sup> affected the neuronal centers of PNEI system. Following Angiobiopathy<sup>v</sup>, then, this causes microcirculatory remodeling, first expression of tumor event, called Inherited Real Risk (RR) of cancer, when both DNA's mutation (nuclear and mitochondrial one) last long enough during which the cell physiologically heals 'crazy', repairs the damage of DNA, or die.

Real Risk (RR) means any mutation, limited at level of cells belonging to a well-defined biological system - for example, beta cells of islets of Langerhans, for diabetes - which occurs in one or more cells when ATP decreases strongly for any reason.

### **a) Vasomotility and vasomotion evaluation**

In Appendix A some elements of Clinical Microangiology useful to understand the evaluation of vasomotility and vasomotion and their meaning are shown.

For the aims of this paper we have to focus on the main concepts of 'Microcirculatory Activation', and normal Microcirculation at rest. As shown in the next chapter, as a consequence of a diagnosis of OT and 'Inherited Real Risk' of cancer, some preventive therapies are suggested. Depending on the different treatments, we can observe different quantitative and qualitative effects in 'Microcirculatory Activation', useful to understand the efficiency and efficacious of each performing therapy for primary prevention.

## **3 QBS primary and pre-primary prevention: the green therapy**

### **3.1 How to make residual the 'Inherited Real Risk of cancer'**

For those who do not have OT, a primary prevention is not required: they will not be at risk cancer. In these subjects the CAEMH can be present elsewhere, but not in the cells of PNEI system, because there is not OT since birth. Although it was emphasized elsewhere in isolated parenchymal cells, with possible beginning - under environmental influences - of degeneration, the process would remain under the control of the vital physiological defense organ.

On the contrary, for those with OT or latent OT a pre-primary prevention is strongly suggested, even in the absence of RR, as RR in the future might arise due, i.e., to environmental risk factors as smoking and drugs. If a patient is positive for 'Oncological Terrain' - OT, detected by mean of a QBS diagnosis, he/she has the opportunity to make an effective primary prevention, especially in the case of 'Inherited Real Risk' of cancer.

In accordance to Angiobiopathy, improving mitochondrial activity in the parenchyma and in microvessel cells, favorably intracellular free energy is involved and various biological activities

are improved: the microcirculation will be normalized. If the way of being and functioning of the microcirculation improves, this means that the way of being and functioning of its parenchyma is also improved. This is done by stimulating the activity of mitochondria by acting on the vehicles as metabolism (chemical process), peptides' net (electric-electronic process), but also improving, normalizing tissue oxygenation, expression of the normal operation of mitochondrial oxidative phosphorylation. Indeed, the mitochondrial functional cytopathy is the *sine qua non* of more frequent and severe human disease and not. For this aim the suggested preventive therapy, called 'green therapy' or type A therapy to distinguish it from the genetic one introduced in the next chapter, includes a proper diet etymologically understood, conjugated-melatonin [13], NIR-LED, LLT, CQ10.

The green therapy allows to make residual the Inherited Real Risk of cancer, i.e., the Oncological Terrain will not disappear, but the congenital risk of cancer is reduced to minimal term, so it stays at a no dangerous stage in the whole process of Oncogenesis.

### **3.2 Genetic reversibility of Oncological Terrain for future generation**

In case of green therapy, the alteration of mit-DNA, evidenced by the presence of CAEMH, still persists, and this means that it could be transmitted, mostly by mothers, to future generations.

While is almost sure that a mother with positive OT will transmit her mit-DNA's alteration to sons and daughters, what about a mother or future parents both with positive OT under an effective preventive treatment in order to let residual their Inherited Real Risk? What about their children? Will they be born with negative or positive Oncological Terrain? These were the written questions done by Stagnaro [5] in order to understand the reversibility, or not, of mit-DNA's alteration (and of Oncological Terrain) for future generation.

The Stagnaro hypothesis was that '*the alteration of mit-DNA is reversible for future generation*': if future parents, both positive for OT, accept to make an effective preventive therapy before procreation, their children will be negative for OT, they will never suffer of any cancer, both solid and liquid, of what studied by QBS.

This conjecture - reversibility of mit-DNA alteration for future generation – formulated by Stagnaro in 2004 has been confirmed in 2010 [14, 15]. This experimental evidence has been called 'Manuel's Story'<sup>2</sup>.

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<sup>2</sup> In April 2010, Manuel is the first newborn in the world NEGATIVE for Oncological Terrain even if both parents are POSITIVE Oncological Terrain. In spite of the fact he is son of mother and father both involved by Oncological Terrain, his parents underwent to a Conjugated-Melatonin treatment a lot of months before pregnancy begins. Technically speaking, his parents became positive exclusively for the residual variant form of predisposition to malignancy, which is not dangerous at all, because mitochondrial respiratory chain is perfectly functioning, so that endogenous-cellular energy level in every biological system results high. Broadly speaking, under preventive therapy, their Inherited Real Risk of cancer became residual, even if they persist to be positive for OT: this means that they can continue to live without any risk of cancer appear. Furthermore their son is negative for OT: this means that his son hasn't got any OT, and of course no real risk of cancer, therefore he does not need of any preventive therapy: none of the tumors studied by QBS will never hurt him in life. The first experimental evidence confirms that Stagnaro's conjecture was true. A widely experimental research could confirm the truth, or not, of this conjecture for a wide range of study cases under a green therapy according with Manuel's story.

## 4 Genetic reversibility and pre-primary prevention: the blue therapy

### 4.1 Latency time of G.A.R.: before, during and after blue therapy

Stagnaro [3] let us another open question: is ‘Oncological Terrain’ reversible? We have seen in the previous chapter that through the green therapy a genetic reversibility for future generations is possible, but this could not be enough for the current generations, especially under environmental negative conditions. QBS tools are not only useful for diagnostic purposes, but also for therapeutic advices, because they are able to measure the microcirculatory activity before and after each preventive therapy’s treatment, in order to understand the effectiveness of remedies.

QBS has recently tested some treatments not yet experimented for preventive purposes as the quantum therapy and the thermal one, and called type B therapy or ‘blue therapy’ [16]. We consider, among the several diagnostic parameters provided from QBS, the ‘Latency time’ (Lt) of the SST-TH ‘Gastric Aspecific Reflex’, as illustrated in Chapter 2.1. In this case the physiological Lt is 8 seconds (NN = 8). If the basal value is less than 8 seconds, then there is ‘Oncological Terrain’ and ‘Inherited Real Risk’ of cancer (Table 2).

Under a continuative type A preventive or green therapy the Lt rises to 12 seconds, so that the Real Risk of cancer becomes residual. By this way tissue oxygenation and mitochondrial activity are improved, mitochondria are running well, but it remains the genetic alteration of mit-DNA (CAEMH and ‘Oncological Terrain’ are still positive). The news is given by the blue therapy, as follows.

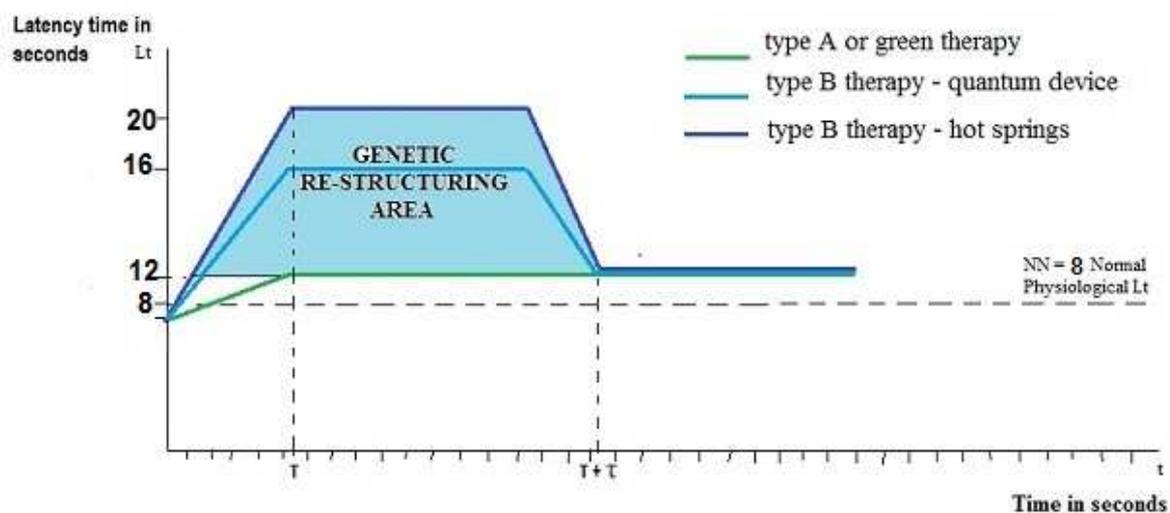
We capture the ‘SST-RH (OT trigger points) frequencies for one minute by means of a quantum device, then we apply the device’s crystals with the customized frequencies, on the same trigger points for 10 minutes. At this point the experimental and clinical evidences done trough QBS diagnosis on more than 30 subjects at Risk of cancer confirms that the ‘Oncological Terrain’ is disappeared. From this moment we observe a very high Microcirculatory Activity type I associated [Appendix A], never seen before, denoted by a Lt of 16 seconds.

After a re-structuring period of time (7 days) the Lt slows down to 12 seconds (more than physiological one). All QBS parameters from the beginning of the application, till the time-out of genetic re-structuring time, and all QBS diagnosis after weeks or months confirm the negativity of Oncological Terrain.

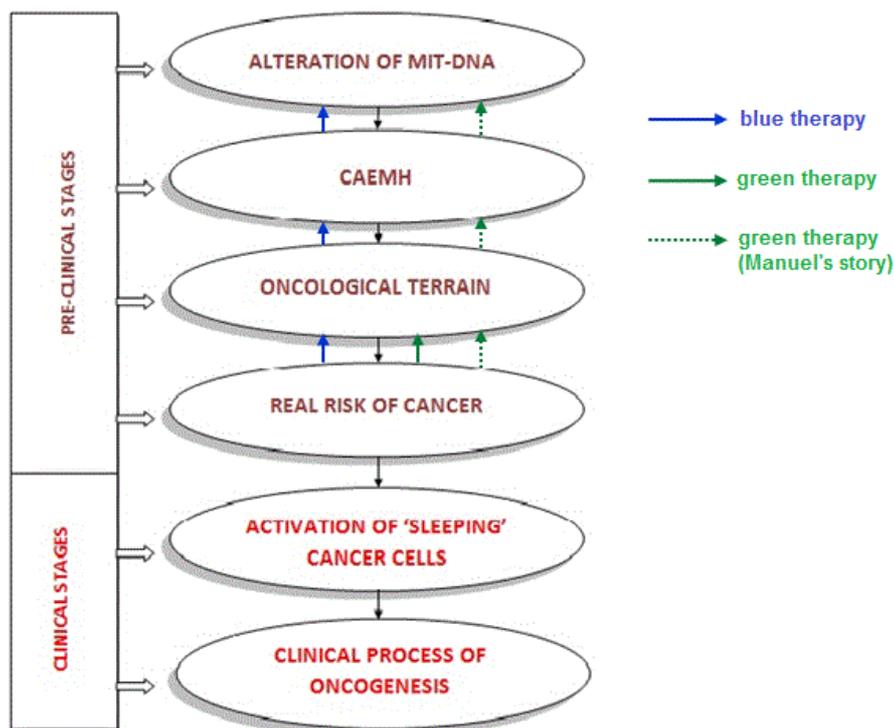
Furthermore, we discover that hot springs have great therapeutic properties: by the same way the ‘Oncological Terrain’ disappears drinking sulfuric thermal water, and the QBS parametrical values are even better than quantum treatment: Lt during the genetic re-structuring length of time rises to 20 seconds, before normalizing to 12 seconds (Scheme 4, Scheme 5).

Diagnosis	OT and IRR of cancer Basal Value	NN - health	Under Green Therapy	During Blue Therapy (Quantum-device)	During Blue Therapy (Spring Water)	After Blue Therapy
Gastric Aspecific Reflex - Latency Time	< 8	8	12	16	20	12

Table 2



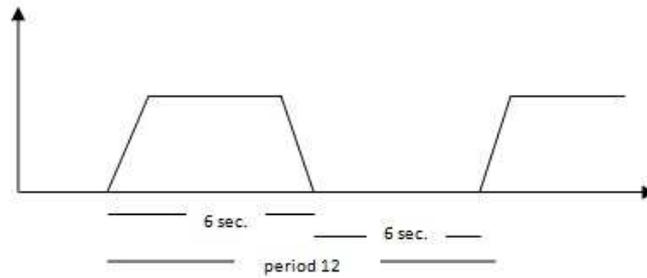
Scheme 4



Scheme 5. The process of Oncogenesis: genetic reversibility

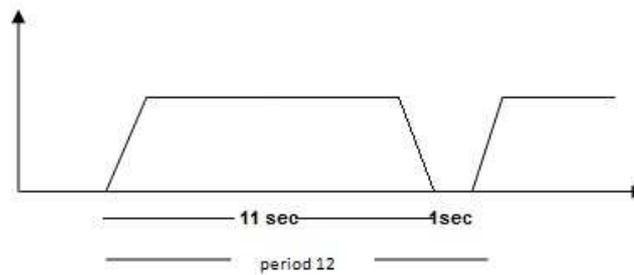
#### 4.2 Microcircle before, during and after blue therapy

The basal value of microcircle, i.e., the duration of the first upper ureteral reflex under light pressure on parenchyma trigger points lasts for 6 seconds, and then follows a pause of 6 seconds, before appearing the second reflex. The period is given by summing the duration and the pause, so we observe a period of 12 seconds (Scheme 6).



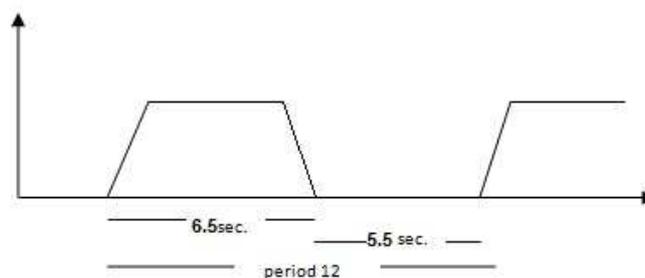
*Scheme 6*

As seen in the previous chapter, the blue therapy allows a genetic restructuring time of length  $T$ , i.e., 7 days. During  $T$ , the reflex duration is of 11 seconds, the maximal value of 'Microcirculatory Activation' never observed before, the pause is of just 1 second, before appearing the second reflex. The period is constantly of 12 seconds (Scheme 7).



*Scheme 7*

At the end of  $T$ , genetic restructuring time of the microcircle, the duration of the first reflex upper ureteral reflex slows and stabilizes, in the 7th day to 6.5 seconds, than a pause of 5.5 seconds follows, confirming a constant and stable period of 12 seconds (Scheme 8).



*Scheme 8*

At the end of the genetic re-structuration, the duration of dilatation of the microcirculation does not return to the baseline (6 seconds), but it stabilizes at a slightly higher value. This remaining extra-work, observed from the seventh day, according to the authors, indicates that once the restructuring took place (the normalization of the stoichiometry of the atoms, the angular effect of various protein of mit-DNA and n-DNA, etc.) a tendency to de-structuring still remains, which is effectively combated by the genome, both mitochondrial and nuclear one, which has well learned the lesson and it works a little more to preserve and stabilize the re-structuration, becoming functionally and structurally useful to the organism itself, in terms of preservation and prevention.

## 5 Conclusions

QBS has been related to the 'Principle of Recursive Fractal Genome Function' (PRFGF) introduced by Pellionisz, in order to understand if the genetic alteration of mit- DNA could be reversed, due to the recursive energy, information and communication feedback between DNA, RNA and downstream structures such as tissues, cells, mitochondria and proteins. QBS clinical and experimental evidences are consistent with and fully confirm the PRFGF, demonstrating, from the clinical view-point, that PRFGF is scientifically right. We argued that the genetic alteration of the mit-DNA is reversible, both under green therapy (for future generations as evidenced by Manuel's story) and particularly under blue therapy (for current generations), which induce the disappearance of 'Oncological Terrain' and the 'Inherited Real Risk' of cancer.

### **APPENDIX A - Elements of Clinical Microangiology**

*According to Tischendorf's concept of Angiobiotopie [17], biological tissue-microvascular system can be described as formed by single units: the tissue-microvascular units.*

*In its turn, the 'Tissue-Microvascular Unit' (T.M.U.) is made up by three fundamental components:*

- 1) microvessels, diameter < 100  $\mu$ ,*
- 2) the blood, flowing in them,*
- 3) perivascular connective, periangium, interstitium or "environment" in which microvessels are placed, formed by water, free- and bound- water, cells and connective fibers, and interstitial matrix, glucosamino-glycanes.*

*Microvessels can be subdivided as follows [18]:*

- 1) Para-microcircle: small arteries and arterioles, according to Hammersen, venules of I, II, III order, shunts or Arterio-Venous Anastomoses (AVA), functionally speaking [19];*
- 2) Microcircle: nutritional capillaries, post-capillaries venules, "meta"- arterioles.*

*With the aid of QBS, doctor is able to evaluate, in dynamic manner, T.M.U. of every biophysical system, from both structural and functional view-point, according to a synergistic<sup>vi</sup> pattern, i.e. the clinical evaluation of microvascular dynamics.*

*Notoriously the microvessels carry on a motor activity, autoctonous and deterministic chaotic, which represents one of the most remarkable manifestations of microcirculatory hemodynamics, characterized by a flow-motion and hematocrit rhythmically fluctuating due to the particular behaviour of both vasomotility and vasomotion<sup>vii</sup>.*

*A biological system, as the tissue-microvessel system, so much highly evolved and well differentiated, as regards anatomy and physiology, cannot react to attacks, different in origin, which involve it, by a lot of ways. As far as tissue-microvessel unit is concerned, cells, transformed in smooth muscle cells and in ramified smooth muscle cells, when stimulated, either contract or dilate, although there is a residual possibility of further response.*

*On the contrary, smooth muscle cells of the media of great arteries – elastic and muscular – which are less differentiated, react to various stimuli, even, de-differentiating and, then, evolving towards cells with secretory activity.*

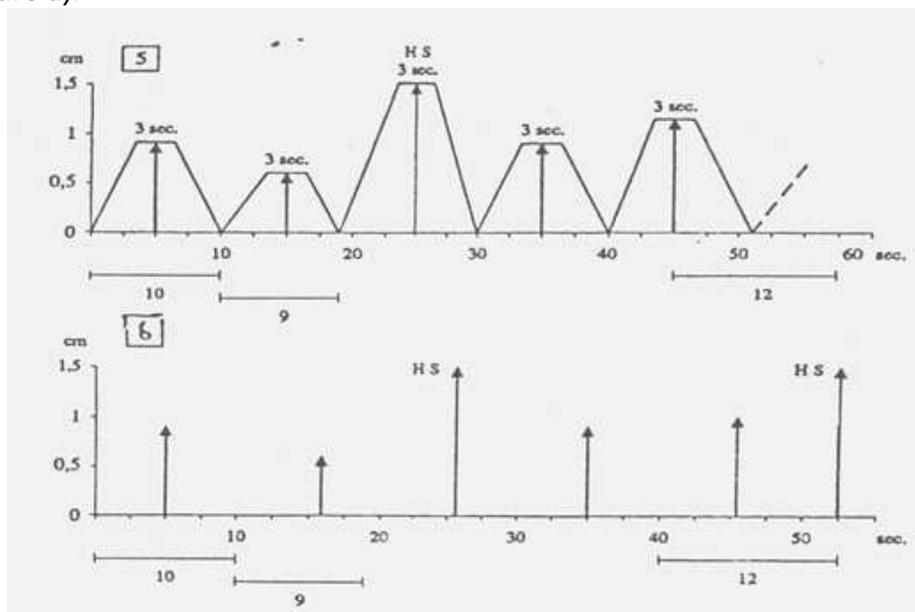
*These concepts account for the reason of the restricted number of 'Tissue-Microvascular Unit' reactions, doctor can observe at the bed-side by biophysical semeiotics and Clinical Microangiology<sup>viii</sup>.*

*According to QBS, in a supine healthy subject, psycho-physically relaxed, with his (her) open eyes, aiming to inhibit melatonin secretion, digital pressure of "low-mean" intensity, applied upon*

the skin projection area ,i.e., of heart, brings about upper, middle, low-ureteral-, gastric aspecific-, caecal-, and choledocic- reflexes, i.e., upper-, mean, low-ureter as well as stomach, caecum, and choledocus dilate, the latter three after a latency time of 8 seconds.

In health, the dilation of upper and low ureteral reflexes, appears after 6 seconds and lasts for 6 seconds, while all other reflex duration is less than 4 seconds. The latter parameter value proved to be of paramount importance, from diagnostic viewpoint, informing precisely about local microvascular structures and function, as well as microvessel remodeling. In fact, such as digital pressure brings about “low-mean” stimulation of coronary trigger-points, inducing “rapidly” oscillations of upper and choledocic reflexes (small arteries, according to Hammersen) and subsequently those of lower urethral (arterioles, nutritional capillaries), which parallel fluctuations of the related microvessel structure, according to a synergetic model.

The oscillations of “upper” reflexes define the vasomotility – the general dynamics of microcirculatory vessels, while those of “lower” one express the vasomotion – capillary- venules dynamics (Figure a).



**Figure a:** Physiology fluctuations of upper and lower ureteral reflexes, at rest (vasomotility and vasomotion); HS stands for Highest Spike or highest oscillation

In Figure a we can see how are practically evaluated vasomotility and vasomotion. Drawing a Cartesian diagram, in the x-axis is represented the reflex’s duration (in seconds), while in y-axis is represented the reflex’s intensity (dilation of parenchyma, in cm).

The normal microcirculation at rest can become physiologically active when the parenchyma starts to work. The important set of microvascular dynamic events, related to microcirculatory activation - M.A., can be subdivided in three types (Figure b):

- type I or “associated”, “physiological”, in which both the vasomotility and vasomotion result increased and consequently blood-flow in nutritional capillaries and post-capillary-venules is augmented, due also to right AVA reaction; (e.g. during parenchyma work);
- type II or “dissociated”, “pathological”, in which the vasomotility shows increasing of both intensity and oscillation duration, while the vasomotion shows a highly differentiated behaviour, in relation to the presence of microcirculatory “compensation” or “decompensation” (failure), as we will say later on. (e.g. during pathological conditions);
- type III or “intermediate”, when vasomotility is activated, while vasomotion shows basal activity, and hemoderivative structures are not activated. The transition from type I to type

It goes through numerous intermediate stages, which from the compensation reach the total irreversible decompensation of microcirculation, showing a large variety of different and significant forms.

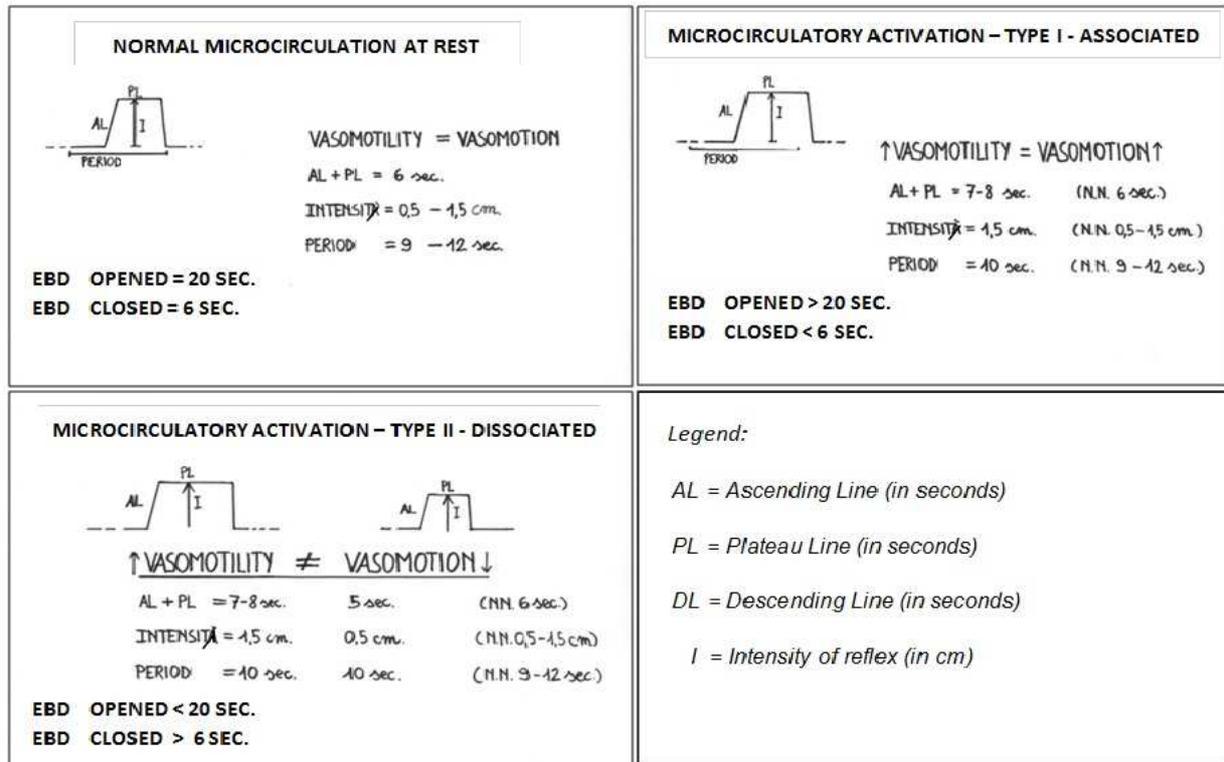


Figure b. Vasomotility and vasomotion. Microcirculatory activation types

M.A. - type I shows the increasing of oscillation waves: the sum of AL<sup>x</sup> (ascending line) and PL<sup>x</sup> (plateau line) duration is equal to 7-8 seconds, maximal intensity (1.5 cm) as well as a period of 10 seconds. Arrows indicate the activation<sup>x</sup> of both vasomotility and vasomotion. Consequently, fractal dimension appears clearly reduced. The under curve area "shows" microvessel sagittal surface during their highest and prolonged opening phase so that, under such condition, microcirculatory blood-flow is greatest.

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<sup>i</sup> Biophysical semeiotic constitutions, detectable since birth, are the inherited congenital ground or terrain of well defined potential diseases clinically hidden, which can last several years before appearing, in the slow transformation process from potential (pre-metabolic syndrome, pre-clinical stages) to effective pathology (metabolic syndrome)

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<sup>ii</sup> Real Risk – RR - means any mutation, limited at level of cells belonging to a well-defined biological system - for example, beta cells of islets of Langerhans, for diabetes - which occurs in one or more cells when energy information EI ( and ATP) decreases strongly for any reason.

<sup>iii</sup> Metabolic syndrome is a combination of medical disorders that increase the risk of developing diseases. The pre-metabolic syndrome, as defined by Stagnaro, is the syndrome that precedes the metabolic one, and is linked with congenital real risks and their associated biophysical semiotics constitutions.

<sup>iv</sup> There are n – DNA alteration, for example, in Oncological Terrain. However, if we correct the functional mitochondrial error (CAEMH) with melatonin, NIR-LED and regular life, diseases do not usually occur. Then, the onset of diseases such as diabetes, cancer, hypertension, is observed when – in presence of n-DNA alteration – the EV decreases (tissue acidosis), but is possible to correct by increase of EV (mitochondria that work well) and consequently increasing the EI (restoring the non-local reality) and disease does not arise at least in most cases. Alteration of the genome requires the reduced EI!

<sup>v</sup> See <http://www.semeioticabiofisica.it>

<sup>vi</sup> The *synergetics* enables us to study the relation between microscopic level and the macroscopic one, with the principle of “self-organization”. This is possible exclusively if, at microscopic level, complex system can modify in qualitative manner; let’s think about the fluids in Bènard’s cells and the laser. Technically speaking, we define “order parameters” macroscopic observables, which describe the macroscopic behaviour of a system, and “enslavement principle” the behaviour of microscopic elements, according to which it becomes defined when originate “macroscopic observables”.

The laser gives us the best example, that illustrates the general rule: the casual emission of waves, under a defined current supply, becomes coherent; when it is exceeded, however, the emission moves toward a deterministic chaotic behaviour. The synergetics, therefore, studies the characteristics of “complex” systems, without considering the nature of their elements, outlining strict analogies between the macroscopic behaviour of the complex systems in spite of the fact that they are really different.

<sup>vii</sup> In all tissues, a part from their local different architecture, microvessel diameter oscillates rhythmically during time. The term *vasomotility* refers to small arteries and arterioles sphygmicity, according to Hammersen, and *vasomotion* is the subsequent oscillation of capillaries and post-capillaries venules diameter.

<sup>viii</sup> Book in progress. See [http://www.semeioticabiofisica.it/microangiologia/common\\_eng.htm](http://www.semeioticabiofisica.it/microangiologia/common_eng.htm)

<sup>ix</sup> It is called ascending line because the reflex’ intensity is growing for few seconds.

<sup>x</sup> It is called plateau line because reflex’ intensity is steady for few seconds.

<sup>xi</sup> Microvessels with diameter of 100  $\mu$  show a motor activity of 2-3 circles/min. and diameter oscillation intensity of 10-20%. As far as vascular diameter lowers, motor activity progressively becomes more intense and rapid; in terminal arterioles, the frequency is 10-20 circles/min. and the width can reach 100% of mean diameter, causing periodically opening and closure of the microvessel.

This rhythmic activity is mainly spontaneous and direct consequence of periodic contraction of smooth muscle cells of arterioles with 20-90  $\mu$  of diameter. Diameter oscillations of small vessels is due to the properties of smooth muscle cells, which have a labile membrane potential and, then, depolarize periodically.

Smooth muscle cells activation by well-known polarization-depolarization processes, which bring about periodic vasoconstrictions, is caused by nervous, hormonal, local biochemical stimuli and also by myogenic stimuli, characteristic of myocytes. These stimuli provoke in smooth muscle cells of small arteries and arterioles, according to Hammersen, the onset of depolarization and consequent ionic fluxes and, then, intracellular storage of  $Ca^{++}$ , partially due to release from cytoplasmic and membraneous storages, which bring about the phosphorylation of myosine, that in turn interact with actine, to start contraction mechanism in presence of phosphorylated nucleotides with high caloric content, produced in mitochondria.

The “vasomotion” varies in relation to temperature fluctuation,  $O_2$  concentration, pH variations, ionic concentration of vascular wall. In fact, it has been demonstrated that  $Ca^{++}$  and  $K^+$  fluxes, due to channels voltage-dependent and, respectively, voltage and calcium dependent, at the base of the periodicity of these transports, brings about the rhythm of arteriolar contractions, ruled also by transmural pressure (Gonzalez-Fernandez J.M., Ermentrout B. On the origin and dynamics of the vasomotion of small arteries. *Mathematical Biosciences*. 119, 127-167,1994).