FUNDING 3D-CBS:
A BREAKTHROUGH TECHNOLOGY, SAFE FOR SCREENING AND EFFICACIOUS FOR EARLY CANCER DETECTION

DARIO B. CROSETTO

Crosetto Foundation - 900 Hideaway Place, DeSoto, TX 75115, USA
E-mail:info@crosettofoundation.com – www.crosettofoundation.org

The role of Positron Emission Technology (PET) should be changed with use of the 3D-CBS (Three Dimensional Complete Body Screening) for maximizing the capture of signals that will detect minimum abnormal metabolism (or other biological processes), achievable by capturing simultaneously and accurately as many signals as possible from the tumor markers from all organs of the body in order to identify the smallest anomaly, at the lowest cost per signal captured and requiring the minimum radiation to the patient. This paper provides scientific arguments for setting new parameters for industry to establish the correct relation between the goal of obtaining substantial reduction in cancer deaths and the implementation of innovations and technology that will provide the expected results through early cancer detection.

1. Introduction

1.1. *Facts & Figures - dimensions of the problem*

In the 38 industrialized countries, listed as those with “Very High Human Development” [1] with a total population of 989 million,

the total cost of cancer is $741 billion/year.

This cost has been calculated as the total cost of cancer[a] in the U.S. in 2008 at $228.1 billion divided by U.S. population as of July 1st, 2008 of 304 million [2]

equals $750/per-capita annually.

---

[a] $228.1 billion total, split as $93.2 billion for direct medical costs (total of all health expenditures); $18.8 billion for indirect morbidity costs (cost of lost productivity due to illness); and $116.1 billion for indirect mortality costs (cost of lost productivity due to premature death).

While estimates indicate that the total cost of cancer[b] in Texas in 2007 was $21.9 billion. This cost divided by a Texas population of 24 million is

> ***$912/per-capita annually (Texas), which is even higher than the $750 for the rest of the nation [3].***

Despite such high costs, every year among this population of 989 million of the 38 most industrialized countries[c], cancer takes the highest toll of

> ***one million/year premature deaths just considering the group 50 to 75 years of age,***

more than any other disease, war or calamity (see National Vital Statistics Report NVSS-nchs showing the constant death rate of 300,000 deaths/year among the group 50 to 75 years of age, among a population of 300 million [4]). The $741 billion/year spent seems not to be very effective because

> ***during the past 50 years reduction in cancer death was recorded as merely 5%***

(as reported by *The New York Times*, April 24, 2009 [5]), while for the same period a **64% death reduction was recorded for cardiovascular diseases** although less investment in research was allocated.

There is too little return of investment, costs are far too high!

> ***Direct medical cancer cost in the U.S. was $1.2 billion in 1963 [6] and jumped to $93.2 billion in 2008 [7]. This is equivalent to 100 times cost increase in 50 years***

(in comparison: bacon went from $0.79/lb to $2.99/lb; eggs from $0.55 dozen to $1.29/dozen; bananas from $0.10/lb to $0.39/lb, etc.).

> *The fact that the* ***premature cancer death rate is not much different in less developed countries*** *that do not have a cost of $741 billion/year proves that the direction in cancer research needs to be changed to make it more efficacious***.**

---

[b] The total cost of cancer in Texas in 2007 was $21.9 billion. Direct cost was $10.0 billion, with $7.7 billion for cancer health care. The indirect cost of cancer due to morbidity and mortality was estimated at $11.8 billion. Cost of cancer-related programs in Texas from State agencies, non-profits and foundations was approximately $78.5 million

[c] The 38 most industrialized countries listed by the Human Development Index (HDI) are: 1. Norway, 2. Australia, 3. Iceland, 4. Canada, 5. Ireland, 6. The Netherlands, 7. Sweden, 8. France, 9. Switzerland, 10. Japan, 11. Luxemburg, 12. Finland, 13. United States, 14. Austria, 15. Spain, 16. Denmark, 17. Belgium, 18. Italy, 19. Liechtenstein, 20. New Zealand, 21. United Kingdom, 22. Germany, 23.Singapore, 24. Hong Kong, 25. Greece, 26. South Korea, 27. Israel, 28. Andorra, 29. Slovenia, 30. Brunei, 31. Kuwait, 32. Cyprus, 33. Qatar, 34. Portugal, 35. United Arab Emirates, 36. Czech Republic, 37. Barbados, 38. Malta

In 1993 a major scientific review
of a breakthrough technology

invented by the author, the basis for a substantial reduction in premature cancer deaths, (at least a reduction of 33%, at a lower cost for each life saved compared to current costs) that would already have been achieved if funded,

was recognized valuable by an international review panel of scientists

from major research centers (FERMIlab, CERN, etc.), from the most prestigious universities (Chicago, Michigan, Irvine, etc.) and from leading industry (Digital Equipment Corp).

The review requested by the Director of the Superconducting Super Collider –SSC- (also Director of FERMIlab) held at FERMI National Laboratory (Batavia, IL) on December 14, 1993, started with a presentation of the innovation by the author at the auditorium of FERMIlab before all scientists and continued for the entire day before the review panel.

A final report compiled on January 31, 1994 recognized the value of the author's invention stating: "*The committee finds this project an interesting and unique concept…*" The review panel, therefore recommended **assignment of all funds available** during the SSC closeout phase ($150,000) to support the author and his research for six months, "t*o complete the current development and leave the project in a state where it could be continued…*"

Since the author's invention passed the review and the project was brought to a state "where it could be continued"' the responsibility from that point on was that of decision makers who manage taxpayer money by awarding grants.

Surprisingly, 17 years after the invention was recognized and approved, and during the past 12 years, during which the author submitted proposals to implement ALL his inventions related to medical imaging for early cancer detection, no funds were awarded. Not even 0.0002%[d] of the cancer cost of 12 years in the 38 industrialized countries.

---

[d] It would have been sufficient to divert 0.0002% (approx. $15 million) from the $8 trillion cancer cost in 12 years calculated as the average cost of $690 billion/year times 12 years. The inventor prepared a detailed business plan showing that with $15 million, three 3D-CBS devices could be built in 36 months, proving in health care facilities in three independent locations that his claimed reduction of premature cancer deaths by 33% at a lower cost per each life saved could be achieved in less than six years. In comparison, $8 trillion cancer cost in 12 years achieved less than 2% cancer deaths reduction at a very high cost per life saved compared to the 33% achievable had the inventions been funded.

> ***If only 0.0002% of those $8 trillion cancer cost during the past 12 years had been diverted to such an award, it would have resulted in over 33% reduction in cancer deaths instead of the 2% realized.***

Here is the untold story of how the benefits of many lives and costs that could have been saved continue to be missed. Included are descriptions of the inventor's claims, the supporting logic, the rationale, initial denial and even admissions that the author's claims were correct as reported in testimonials by academia and industry.

The rationale for the invention that contributes to progress to the benefit of mankind [8] as already explained, recognized and approved elsewhere [9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30] will be highlighted. In 1992 the author, in one month, presented his innovation at three international conferences in Europe and the U.S. and two of his articles were published in the peer reviewed scientific journal *Nuclear Instrument and Methods in Physics Research*, while the following year he passed a major international scientific review on December 14, 1993 at FERMIlab. His innovation was recognized valuable and adopted by large collaborations of hundreds of scientists (GEM at SSC in 1993 and LHCb at CERN in 1995) and was included in their respective Technical Design Reports [15, 18]. Unfortunately, in both cases the U.S. Department of Energy suddenly stopped funding the overall projects for reasons unrelated to science and consequently funding for the author's project was no longer available.

Finally, with respect to the medical imaging application, the obstacles that need to be removed in order to bring the benefits of ALL the author's innovations to the bed of the patient will also be made clear.

1.2. *What is Cancer?*

Cancer is a disease characterized by the **mutation of normal body cells** into cancerous cells whose main characteristic is out of control reproduction, increasing in volume to the detriment of neighboring tissues, also invading other distant tissue, transported through the blood vessels (metastasis).

Normal cells become cancer cells due to DNA damage. Instead of dying, cancer cells outlive normal cells and keep forming new abnormal cells with the same DNA damage as the first cells. Their shape is different due to a different ratio between nucleus and cytoplasm and their structure is irregular. Because they grow faster, **cancer cells need more nutrient** (up to 70 times more than normal) thus showing abnormal metabolism.

1.3. *What causes cancer?*

We know many causes of cancer. The main ones are: heritage, chemical products (smoke), virus, bacteria, radiation, etc. However, we do not know all of them and most importantly **we cannot know when cancer starts developing,** therefore the most effective way to fight it is to be vigilant, by monitoring through screening people at high risk of cancer because of their age, heavy smoking, heritage, environmental conditions, etc.

1.4. *How has the cancer calamity been addressed?*

Cancer is a serious calamity affecting over 40% of the world population during their lifetime and over 10% will die prematurely due to that disease.

In the face of such a calamity that causes more premature deaths annually than any war, and therefore which should be enemy number one, we (the world) are still losing this battle perhaps because a gigantic strategic error is being made.

During the past half century, although enormous investments have been made (in the United States alone, $8 billion/year for research and $64 billion/year, mainly for the cure of late stage cancer [7]), the cancer calamity has been almost exclusively addressed through the study and development of new drugs and therapies targeted to the cure of cancer diagnosed at a late stage. As has been noted, these investments have yielded meager results in terms of a reduction in recent years in cancer deaths of less than 2%.

1.5. *How should the cancer calamity be addressed?*

Experimental data confirm that **cancer diagnosed at an early stage has 90% to 98% probability of resulting in a life saved**. (Diagnosis at a late stage for lung cancer, the number one killer, shows a survival rate of less than 10%).

These data refer to cancer incidence and survival in the United States recorded between 1960-2004, compiled by Surveillance Epidemiology, and End Results (SEER), a program of the National Cancer Institute (NCI). Reference tables [31] for Lung, Colon, Breast and Prostate cancers, summarized on the final page indicate that for prostate cancer, 91% were detected at an early stage and 100% of these survived, but for lung cancer, only 16% were detected at an early stage and of those 49.5% survived.

These figures for lung cancer clearly show that no early efficacious detection is available. But when, in those 16% of cases, it is detected early, there is a good chance for survival of 49.5%. Unfortunately, for the 51% of cases when lung cancer is detected at a late stage, only 2.8% survive for a 5 year period. For breast and colon cancer, data from those SEER tables show that early detection provide 98.1% and 89.7% survival rates respectively.

Clearly these data demonstrate that early detection saves lives.

The general public is informed about these results without the necessity to study raw data from SEER table reports or scientific journals, but are able to review comprehensible graphs published in magazines such as FORTUNE [32] and WIRED [33]. Therefore, it is puzzling that they do not

> ***demand greater investment of their tax dollars in early cancer detection which is shown to be effective***

while the cure for cancer detected at a late stage does not work in most cases.

These experimental data show that it is necessary to realign research toward early cancer detection to achieve the capability of capturing the first signals that show the start of a mutation of normal body cells into cancerous cells rather than to focus almost exclusively on the development of drugs and therapies targeted to the cure of cancer at an advanced stage.

In order to understand **which signals are important to be detected**, it is necessary to know how cancer initially manifests itself.

2. How does cancer manifest itself?

Cancerous cells, can be differentiated from normal cells through detection of signals that provide information about cell mutation.

> ***Such signals are related to changes in: odor, temperature, tissue density, fluorescence, metabolism, perfusion, etc.***

Although it is important to use the information provided from several of these signals (obtained from several individual instruments such as Ultrasound, X-ray, CT or in multimodality such as: PET/CT, PET/MRI, etc.) and not rely only on one of them, some signals provide more reliable information than others. The agreement in indicating the presence of cancer cells by several of them will contribute, together with the experience of the physician, to a correct diagnosis that will ultimately be confirmed by biopsy.

Among all these signals, the one most reliable and useful for early detection and for reduction of "false positives" and "false negatives" is the change in metabolism (up to 70 times higher in cancerous cells) and other biological processes, **those that provide information at the molecular level**, even before symptoms or morphological changes (change in tissue density) occur.

The other signals are less reliable for the following reasons:

1. change in odor is unreliable and is not related just to development of cancerous cells
2. it poses a technical problem to create temperature and fluorescence maps of the body for areas deeper than about 5-mm from skin surface
3. some cancers develop without changing density. Therefore even a perfect CT, MRI, Ultrasound, X-ray, etc. measuring changes in tissue density cannot detect cancer in those cases. Current diagnostic devices mentioned above (including mammography) based on tissue density measurement require the presence of many cancerous cells in order to detect them (there are about 1 billion cells in 1 cm^3), at a stage of development that cannot be called "early detection."

3. What is the technological limit in current diagnostic equipment to identify the very first cell mutation (early detection)?

Among all techniques to detect signals generated by body cell mutation (odor, temp., etc.), **the technique that provides the best signals is the one showing abnormal biological processes at the molecular level.**

> ***This technique called 'positron emission technology' needs to capture, accurately measure and count all possible signals emitted from the decay of a radioisotope integrated in the molecule of a tracer.***

All other techniques that are not based on direct measurement at the molecular level (although some are used for functional imaging with indirect measurement of biological processes, such as fMRI and CT with contrast agents) such as X-ray, CT, Ultrasound, Mammogram, etc. They are **limited** by not being able to show cancer development which does not involve tissue density changes, and, in the event there is a change in tissue density, are unable to provide early detection because several million (or billion) cancerous cells need to be present before these devices can detect them.

One important application of positron emission technology is **measuring changes in metabolism** at the molecular level by capturing, measuring the property of and counting in a unit of time the signals emitted from the radioactive tracer integrated in the molecule of the nutrient to the body cells (see Figure 1).

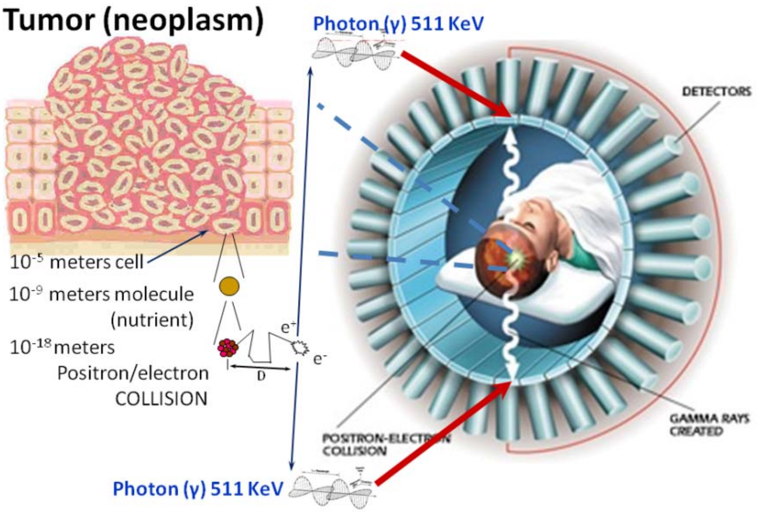


Figure 1 Representation of the principle of operation of Positron Emission Technology. Cancerous tissue (neoplasm) is identified by its natural nutrient uptake (for example: glucose molecules) labeled with a radionuclide. The positron e^+ emitted by the radionuclide, after traveling for a distance D, annihilates (collides with) an electron generating two photons that are emitted in opposite directions. These pairs of photons (or gamma rays) hit two locations on the detector almost at the same time (called in-time coincidence). The task is to capture and accurately measure (energy, arrival time and x, y, z coordinates) as many as possible of the emitted 511 KeV photon pairs in-time coincidence that reveal the concentration quantity of the radioisotopes (or nutrient in the body cells). The goal is not just to capture as many as possible of the 511 KeV photons emitted from the patient's body, which provides the benefits of early detection and lowering the amount of radiation needed to be administered to the patient, but also does this at the lowest possible cost per each 511 KeV photon captured.

The technique works by injecting into the bloodstream, swallowing or inhaling as a gas a nutrient compound (molecules of glucose, oxygen, carbon, etc.) tagged with a radioisotope (tracer) to be taken up by the body cells and monitoring its path and where it accumulates within the patient's body by means of a device that can capture signals emitted (photon pairs) by the decay of the radioisotope. Because cancerous cells take up to 70 times more nutrient than normal cells, positron emission technology allows identification of those cells (or group of cells) that take up more nutrient than normal, thus a suspected cancer site.

Having verified that positron emission technology provides the best signals, one should also realize that the current over 5,000 Positron Emission Tomography (PET) devices that make use of the principle of operation of positron emission technology, due to their low efficiency, cannot provide early detection because they capture and inaccurately measure only one signal out of

10,000 from the tumor markers (and they require administration of a radioactive dose that is over ten times higher than the level recommended as safe for screening asymptomatic people by the International Commission for Radiation Protection, ICRP).

> ***In order to achieve true safe early detection, it is therefore necessary to focus on greatly increasing the efficiency of current PET.***

This will change the current role of PET from that of measuring the dimension of tumors mainly detected at an advanced stage using other procedures, with the limited goal of helping the physician with a prognosis and justifying the use of expensive cures that in most cases will not save lives, to that of a safe screening device for efficacious early detection of the start of cancer development in asymptomatic patients at high risk (or in the restart of activity in cancer survivors). It is this early detection that has been shown to save lives.

The fundamental problem to be solved in order to obtain such improvements is the same as the one already faced in High Energy Physics (HEP) experiments.

3.1. *Description of the fundamental problem relative to the increase in efficiency*

The fundamental problem, relative to the possibility of increasing efficiency, to be solved in Particle Physics was the **impossibility of making accurate measurements on ALL data received from radiation (called events) that arrive at very high data rates from the detector** as the result of millions of collisions between particles generated by accelerators such as the LHC collider, at CERN.

Accurate measurements are necessary in order to distinguish “good events” from those carrying no useful information that are considered as background noise. For example, LHC detectors can have something like 600 billion events per second. If all that data were saved for study at a later time, it would fill up every hard drive on the planet in only one day.

Hence, because of the need to analyze all events in real-time, a sophisticated trigger system was created to analyze, select and save in real-time about one hundred of the highest quality collision events per second (this number of events to be saved is related in HEP to a parameter called “occupancy” for a specific experiment that is estimated by theoretical physicists, whereas in Medical Imaging it is determined by the maximum radiation dose that can safely be given to a patient).

A similar problem also exists in Medical Imaging. In positron emission technology, it is also necessary to sustain a high input data rate of a million events per second arriving from the patient's body to which a radiation dose was administered. It is necessary to analyze all of them in real-time, selecting accurately only the good events generated by the tumor markers and excluding the "scattered events", "randoms", "multiple events" and the so called background noise.

In summary the problem to be solved has the two aspects of being able to:

1. cope with a high input data rate in order to fully use all information carried by the radiation, and
2. accurately analyze all signals in order to identify all good events

The two aspects are related to the efficiency of the system in particle detection. **The solution is much more critical for Medical Imaging than for Particle Physics.** In Particle Physics, inefficiency only causes a delay and a higher cost in discovering new particles.

Much more serious and damaging is inefficiency in Medical Imaging devices because not only is there a **higher cost for health care**, but it also **requires administering a higher radiation dose, dangerous to the patient, does not provide the necessary sensitivity to diagnose cancer at an early stage, and is not accurate enough to be able to reduce "false positives" and "false negatives."**

4. Solution of the fundamental problem: the author's invention relative to the Trigger

The author presented his innovation of a high-performance 3D-Flow [34, 35] programmable, technology independent parallel-processing system to the scientific community in Sept. and Oct. 1992 at three international conferences in Europe at Annecy, France [9], in the United States at Corpus Christi, Texas [10] and IEEE-NSS-MIC in Orlando, Florida [11] where different ideas [36], [37], [38], [39] and approaches to the implementation of trigger systems were discussed. The value of the author's innovation was recognized and approved at the 1993 FERMIlab international scientific review (see Section 1.1), and emeritus scientists in the field wrote letters of recognition (see testimonials at [40]). The 3D-Flow [19, 23] is a parallel-processing system capable of neighboring data correlation with no boundary and of real-time execution of complex algorithms for a time longer than the interval between two consecutive input data. In addition to solving the problem for different HEP experiments, achieving higher performance at a lower cost when compared to the traditional approach, this innovation can detect very accurately all characteristics of 511 KeV pairs of photons in PET Medical Imaging.

Figure 2, shows how the 3D-Flow parallel-processing system allows a processing time for each set of data in a pipeline stage for a time longer than the time interval between two consecutive input sets of data.

In the example, an identical circuit (the 3D-Flow processor) is replicated five times in the 3D-Flow parallel-processing system. (The number of times the circuit is copied is equal to the ratio between the maximum algorithm execution time and the time interval between two consecutive sets of input data). The figure shows an example where the maximum algorithm execution time is 30 seconds and the time interval between two consecutive sets of input data is 6 seconds. (30/6 = 5).

A 3D-Flow Logical Unit is represented in the figure with three functions: a) a “bypass switch” to move data past occupied stages, represented as a long arrow in a rectangular box; b) a “bypass register”, an output register represented as a rectangle to the right of the arrow, and; c) a CPU or Central Processing Unit, represented as a rectangle below the arrow.

A “bypass switch” sends a package of data to its CPU and transfers (“bypasses”) four packages of data to the next stages to the right in the figure.

Table 1 shows the sequence of the packages of data in different times in one 3D-Flow electronic channel. A package of data contains information received at a given time from a “detector channel” of the 3D-CBS (Three-Dimensional Complete Body Screening) detector.

In the first column (on the left side of the table) the time “t” is shown. Values below the columns labeled (Proc (1d), Proc (2d), Proc (3d), Proc (4d) and Proc (5d)) represent the packages of data that are processed by the 3D-Flow processor in the specific time “t”.

Values labeled “ix” and “rx” below columns (Reg (1d), (Reg (2d), (Reg (3d), (Reg (4d) and (Reg (5d)) are respectively input data and output results that flow from register to register in the pipeline chain toward the exit point.

One should note that data-package No. 1 stays in the first processor of the first stage for five cycles, while four data-packages (i2, i3, i4 and i5) are passed forward (via the “bypass switch”) to the next stage.

For example at clock 12t (see Figure 2), while station 4d receives data-package No. 9, at the same time, it outputs results r4 relative to the data processed previously. This result “r4” is then transferred to the output of the 3D-Flow system without being processed by other stages.

Each package of input data stays in a 3D-Flow processor for a time equal to about five times the time interval between one data package and the next.

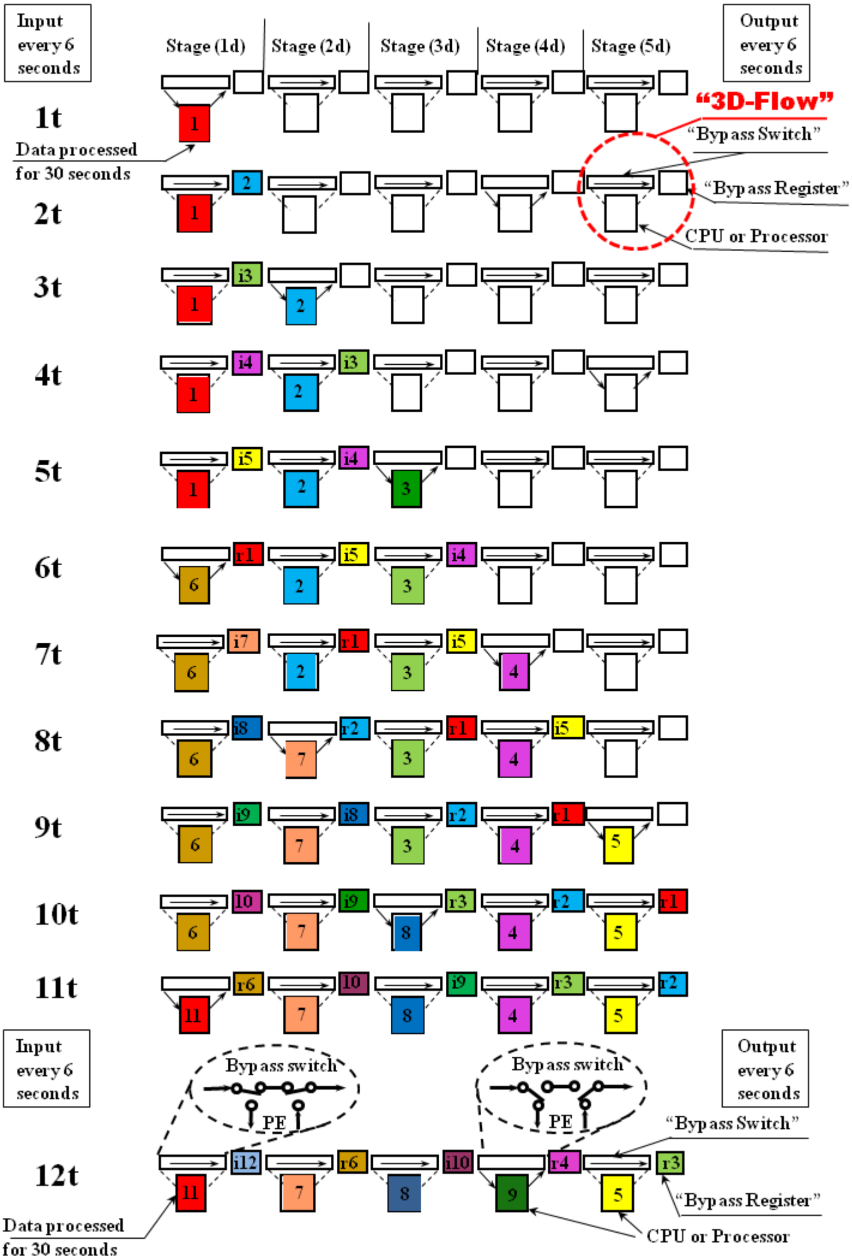
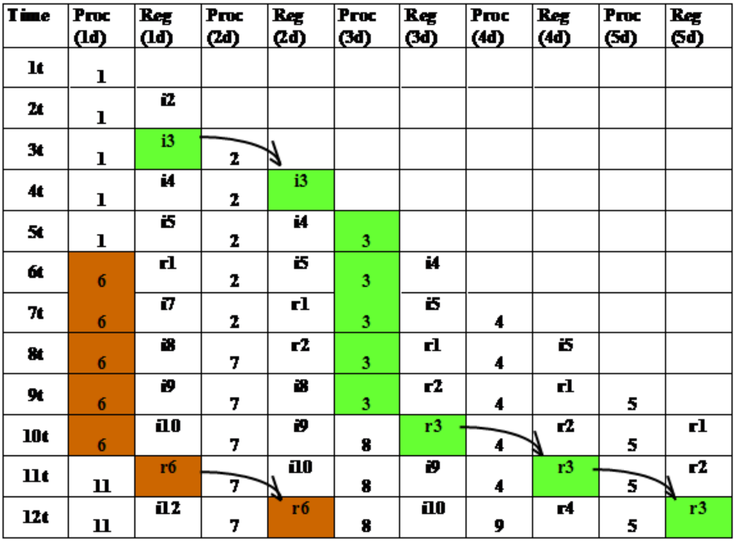


Figure 2. Data flow in one electronic channel of the 3D-Flow parallel-processing system that enables acquiring data at a very high input data rate while simultaneously allowing necessary time to accurately analyze the information.

Table 1. Sequence of the packages of data in different time as they flow in one 3D-Flow electronic channel.



Time	Proc (1d)	Reg (1d)	Proc (2d)	Reg (2d)	Proc (3d)	Reg (3d)	Proc (4d)	Reg (4d)	Proc (5d)	Reg (5d)
1t	1									
2t	1	i2								
3t	1	i3	2							
4t	1	i4	2	i3						
5t	1	i5	2	i4	3					
6t	6	r1	2	i5	3	i4				
7t	6	i7	2	r1	3	i5	4			
8t	6	i8	7	r2	3	r1	4	i5		
9t	6	i9	7	i8	3	r2	4	r1	5	
10t	6	i10	7	i9	8	r3	4	r2	5	r1
11t	11	r6	7	i10	8	i9	4	r3	5	r2
12t	11	i12	7	r6	8	i10	9	r4	5	r3

Unlike a standard pipeline system, the result of a calculation from one processor can never become the input data of another processor located in a subsequent station, but will be transferred to the next stage without being processed further.

4.1. *Validation of the concepts*

The new concepts are proven by logical arguments in articles, [10, 19, 20, 22 23], **by simulation** (see Sections 11, 12 of [19], Appendix of [23], Chapter 13 of [20])**, by construction of the innovative parts in working hardware [26] and by experimental results by third parties (i.e. Siemens [41]) that confirm the author's claims**.

Despite the fact that the author did not receive additional funding after DOE general funding for SSC (1993) and LHCb (1999) was cut for the overall projects, consequently for the author's project, he was able to build his innovative idea in hardware with personal funding and the support of friends.

The first demonstration of the proof of concept was made at the IEEE-NSS-MIC Industrial Exhibition (San Diego, CA) in 2001. At the Industrial Exhibition booth, the author set up the hardware demonstration of circuits and input/output test boards to show the execution of real-time photon detection algorithms, centered on each electronic channel of the processor array (3x3 "local maxima" with no boundary, Depth Of Interaction, DOI, etc.) on the 3D-Flow architecture.

This system was built using two prototype boards from Altera (each accommodating a Field Programmable Gate Array circuit FPGA EP20K1000) interfaced with two other prototype boards, one to input data from switches and another to display results on LED.

Each FPGA accommodated four 3D-Flow processors running at 32 MHz internal clock for the core and at 256 MHz for the I/O. The two FPGA-Altera boards made a two layer 3D-Flow system. The first FPGA board was connected to the input board where the user could select two sets of input pattern of data (configuration of the input switches) that would simulate two subsequent events received from the detector.

External connections (North-South and East-West) to both FPGA chips were made to be able to simulate a 3x3 centroid algorithm. The second FPGA board was connected to the output board where results were displayed on LED showing if a "local maxima" was detected, while signal waveform on the oscilloscope proved the algorithm execution in a given number of steps and at the expected speed.

The proof of concept allowed extraction of the parameters (power consumption, number of processors per board, etc.) to build an industrialized modular system based on IBM PC boards as described in Section 15 at page 156 of [20] and shown in hardware construction in [26].

A 3D-Flow system made of two modular boards with 136 processors that allows expansion using many of the similar modular boards, into a system of infinite dimensions, performed according to expectations at the first version built. Each 3D-Flow DAQ board consists of 2,211 components, over 20,000 contact pins connected through only 8 layers of printed circuit board for signals and 6 layers for power and ground.

5. The 3D-CBS Solution: the author's additional inventions related to early cancer detection

The first milestone leading to the 3D-CBS technology for early cancer detection was the author's basic invention in 1992 of the 3D-Flow system: **a parallel-processing architecture that allows executing complex real-time algorithms with neighboring data correlation for a time longer than the time interval between two consecutive input data without the need to use expensive ultra-fast electronics.**

This invention overcame three stunning obstacles: limits in sustaining high-input data rate, limits in accurately analyzing all input data and limits of high cost electronics. These advantages are described in simple terms with analogies, at page 26 of the article on Planetary Emergencies [29] and also in the video containing an analogy implemented by high school students [42].

The analogy in the video points out that no matter how complex the problem to be solved in the envelope (consequently how much time is required), or at how high a rate the envelopes arrived from the corridor, the students have all the time necessary to solve any complex problem contained in the envelope without the need to rush or take short cuts. The focus is not on the **content** of the envelope at that time. In other words, only the solution for getting more time to address the content of the envelope is explained at that point.

Proof of the benefit of this invention in HEP and PET derives from the fact that after this discovery, approaching the solution of extracting more useful information from radiation (in HEP experiments or PET), filtered from what is called "background noise" using expensive fast GaAs, ECL, 40 nm technology, etc., cabled logic, is no longer justified. Again recently, this scientific truth could not be disputed by scientists at forums on the 3D-CBS innovative technology held September 24, 2009 at Brookhaven National Laboratory, New York and on September 30, 2009, at the Policlinic San Matteo in Pavia, Italy.

Besides overcoming obstacles and reducing costs, **this first invention opened the door to other inventions, both in HEP and in Medical Imaging** in the geometry of the detector, assembly of the crystals and their coupling with transducers, coupling of the detector channels with the electronic channels, using new real-time algorithms, etc., which before could not even be envisioned.

The second milestone of the 3D-CBS technology for early cancer detection, **was the solution that allowed improvement at a lower cost** of the analysis of the parameters to **measure the energy, arrival time and x, y, z coordinates** of the incident photons in the crystal detector and also greatly improved the **signal to noise ratio** that allowed efficacious filtering of noise, in this case, radiation not useful for the diagnosis.

Figure 3 summarizes the author's additional inventions described in more details in the references [20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30].

This second milestone is not merely an invention of a new real-time algorithm or electronics, but several unusual, innovative ideas underlying this system that **require thorough, careful study of the 3D-CBS system as a whole and each of its parts separately**. One cannot just skim over any part and hope to achieve a knowledgeable understanding of a single part, let alone an assessment of the synergy of the entire system.

In the analogy, it is not what deals with the analysis of the problem contained inside the envelope that needs to be solved (not merely a calculation), but, as explained in a second analogy at page 26 in the Erice paper [29], it deals with solving problems of communication among offices, geometry, etc.

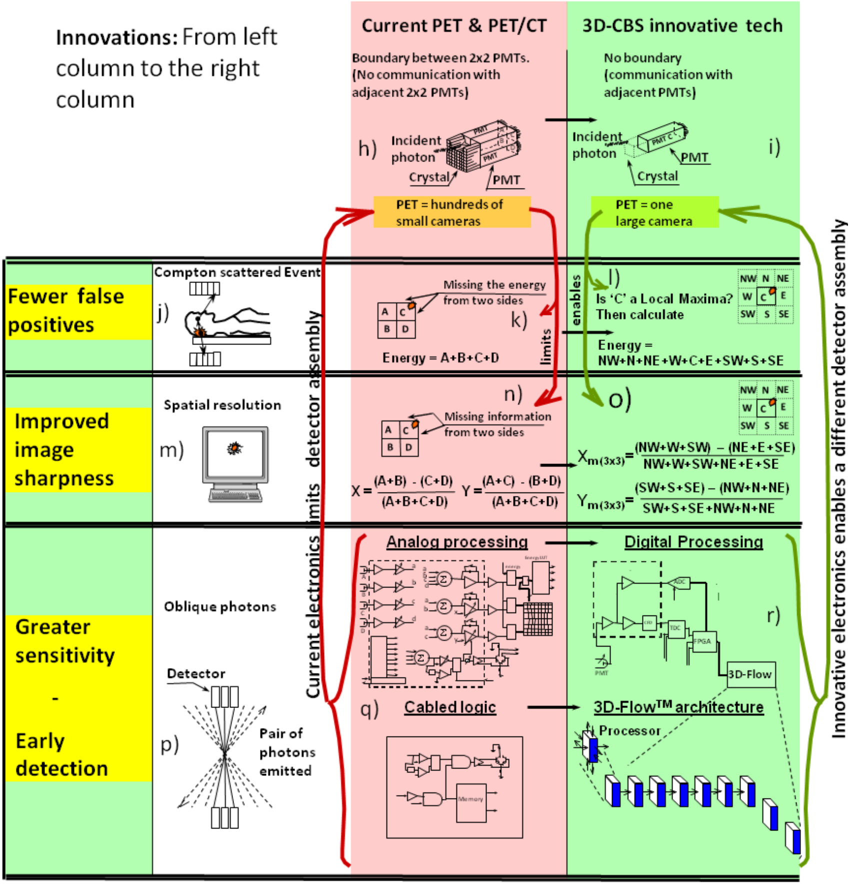


Figure 3 Key innovations of the 3D-CBS technology. The three titles in the left column summarize the advantages of the 3D-CBS with respect to current PET in a language addressed to the doctor/radiologist. In the second column, supporting the statement to the doctor/radiologist is illustrated the corresponding physical phenomenon that make it possible to obtain such advantages. The third column shows the limits of current PET and the last column to the right how such limits are overcome with the 3D-CBS technology. Boxes "j", "k", and "I" concern the energy resolution; "m", "n", and "o" the spatial resolution; and "p", "q", and "r" the sensitivity. The key innovations start from the feature in box "r," which enables the innovation in box "i", which in turn enables the innovations in box "l" and "o." Additional innovations are achieved as a result of synergy of all three, allowing to greatly improve in a cost-effective manner the five parameters listed in Section 6. providing more accurate measurements at a lower cost for each photon captured.

In 2000, the author published scientific articles and books describing the advantages of his innovations in Medical Imaging [19, 20, 21]. These publications first analyze the inefficiency of current PET (Positron Emission Tomography) in Figure 3-4 page 23, [19] (or Figure 3, [24], both showing the ideal vs. actual time coincidence detection of current PET), then analyze the area where photons are lost in current PET in Figure 14-1 on page 136, [19] (or Figure 1, [23]) and provide the solution for capturing more accurately and more cost-efficiently over 400 times the number of positron-electron annihilation photons**.**

Further reviews not only of the innovative electronics but of the entire Three-Dimensional Complete Body Screening (3D-CBS) system took place on several occasions one in 2003, in Dallas, TX (see video at www.3d-computing.com), with the final report by the review panel available at [26]. In 2008 an international review was also conducted in Rome, Italy.

6. How claimed objectives are achieved with the author's innovations

By implementing these two milestone inventions, it is possible to achieve substantial reduction in premature cancer deaths due to significant results in early cancer detection. This is obtainable through screening with a device that is safe for the patient, provides the most accurate information on minimal abnormal metabolism and/or biological process indicating suspected development of cancer (augmented byinformation from other less reliable techniques combined with the extensive experience of the physician and ultimately by verification with a biopsy).

The author's invention, related to the Trigger, has finally solved two aspects of an enormous fundamental problem relative to the increase in efficiency. Until this invention, these two aspects were considered unsolvable in HEP and in Medical Imaging. Because of that, now it is possible to make use of ALL information received from the radiation.

The 3D-CBS technology makes possible building very efficient 3D-CBS devices, capable of distinguishing, very accurately, at the molecular level, cells growing at a regular speed (or not growing) from cells growing at an abnormal speed (the typical behavior of cancerous cells) throughout the body, and recognizing them even when there are a relatively small number (early detection).

The characteristics of the 3D-CBS device permit using a very low radiation dose to perform an examination in a short time at a low cost. Compared to the widely approved mammogram screening based on tissue density measurements requiring the presence of many cancerous cells to be detectable as a tumor, the superior technical characteristics of the 3D-CBS technology, sensitive to changes in biological processes of fewer cells at the molecular level, outperforms mammogram technique. Therefore, 3D-CBS screening of a population at high risk for cancer is greatly justified by the higher number of lives that can saved as well as for the fewer false positives and false negatives due to more accurate measurements.

Progress is achieved by improving accuracy in measurements and its impact is greater if done at a lower cost. The combined innovations of 1992 and the ones announced in 2000 prove achievement of both because each electronic channel that receives information from an area of the detector correlates data with the neighboring element and any complex algorithm can be performed with no limit on time or requiring expensive electronics. For example, the energy calculation summing nine (or 25) elements is more accurate than summing four elements as performed in current PET. Similarly the improved accuracy at a lower cost of each measurement performed with the 3D-CBS technology with respect to current PET can be demonstrated.

In summary, the key elements of the author's innovative technology that allows building a device of the 3D-CBS type relate to five main areas:

1. Increased detector length – longer Field of View (FOV) made possible because of the other innovations that allow the use of more economical crystals without a large increase in cost.
2. Improved and simplified detector assembly.
3. Innovative electronics providing a means of:
    a. accurate identification of the impact point of all photons including the oblique photons and accurate measurement of their total energy;
    b. reduction of the initial number of the electronic channels;
    c. simplification of the method for identifying in-time coincidences.
4. Capability of executing complex algorithms for photon identification.
5. Innovations in the visualization of the information obtained.

The synergy of all these inventions allows capturing more accurately all possible signals from tumor markers at a lower cost for each signal captured providing the physician more accurate measurements of five parameters that allow reduction of "false positives", "false negatives", lower examination cost and enables early diagnosis.

These five parameters are:

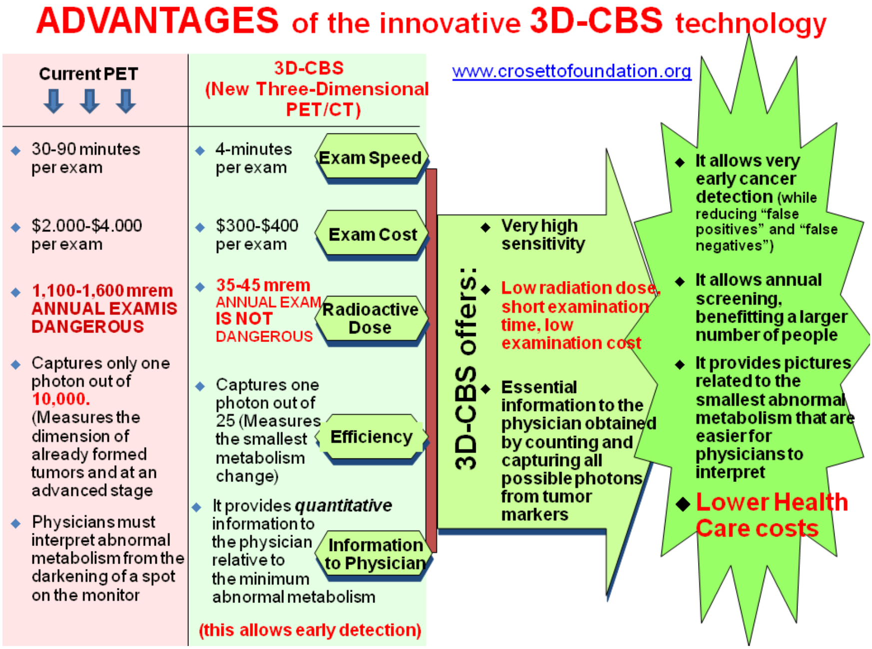
1. Accurate measurement of total photon energy, using the signals received from 9 electronic channels (rather than 4 as used in current PET), that allows discrimination of "good events" from "scatter events".
2. Accurate measurement of the photon arrival time (Time-of-Flight -TOF-) that allows discrimination of "good events" from "randoms" and "multiple" events.

3. Accurate measurement of the spatial resolution referred to the ‘x’ and ‘y’ coordinates (distance in the axial and 90° with respect to the axial direction of the impact of the photon into the surface of the crystal. Centroid calculated based on 3x3 array rather than a 2x2 array as used in current PET)
4. Accurate measurement of the photon Depth Of Interaction (DOI) which allows elimination of the parallax error.
5. The improved signal-to-noise ratio makes it possible because of the capability to execute complex algorithms in real-time, while sustaining at the same time a high input data rate.

7. Summary of the advantages of the innovative 3D-CBS technology compared to current over 5,000 PET

Figure 4 defines “efficiency” used throughout this document and summarizes the advantages of 3D-CBS technology compared to current over 5,000 PET.

$$\text{Efficiency} = \frac{\text{Pairs of photons in time coincidence detected by the instrument}}{\text{Radiation activity in the patient during the scanning time}}$$



ADVANTAGES of the innovative **3D-CBS** technology

www.crosettofoundation.org

Current PET	3D-CBS (New Three-Dimensional PET/CT)	
30-90 minutes per exam	4-minutes per exam	Exam Speed
$2.000-$4.000 per exam	$300-$400 per exam	Exam Cost
1,100-1,600 mrem ANNUAL EXAM IS DANGEROUS	**35-45 mrem** ANNUAL EXAM **IS NOT** DANGEROUS	Radioactive Dose
Captures only one photon out of 10,000. (Measures the dimension of already formed tumors and at an advanced stage	Captures one photon out of 25 (Measures the smallest metabolism change)	Efficiency
Physicians must interpret abnormal metabolism from the darkening of a spot on the monitor	It provides *quantitative* information to the physician relative to the minimum abnormal metabolism	Information to Physician
	(this allows early detection)	

3D-CBS offers:

- Very high sensitivity
- Low radiation dose, short examination time, low examination cost
- Essential information to the physician obtained by counting and capturing all possible photons from tumor markers

- It allows very early cancer detection (while reducing “false positives” and “false negatives”)
- It allows annual screening, benefitting a larger number of people
- It provides pictures related to the smallest abnormal metabolism that are easier for physicians to interpret
- **Lower Health Care costs**

Figure 4 Comparison between the approach used in current PET to measure tumor dimensions at an advanced stage and the new 3D-CBS approach to measure the minimum abnormality in biological processes targeted to early cancer detection

8. Research Strategy

The research strategy is to build a very efficient, cost-effective 3D-CBS device over 1.5 meters in length, according to the basic specification reported in Section 17.1.2, page 176 in the book published in 2000: “400+ times improved PET efficiency for lower-dose radiation, lower-cost cancer screening” [20], just for the PET/CT application (no SPECT section will be considered) modified according to the updates in successive publications [21, 22, 23, 24, 25, 26, 27, 28, 29, 30], for maximum optimization of low cost and high performance.

In order to avoid delay of FDA approval of the CT section that transmits radiation to the patient, a commercial 16-slice CT will be leased or purchased. The CT will operate at very low dose radiation, just to acquire the attenuation coefficient for the correction of the PET data and also to provide the tissue density information that will help to localize the tumor (shown by the PET section of the 3D-CBS device as a hot spot for any abnormal biological activity) within the organs and/or body tissues.

With this initial strategy, there will be no need for FDA approval (ethical approval with consent of the patient should be sufficient) because the 3D-CBS device will just observe the radiation activity emitted by the radioisotope from the patient’s body that for the first tests uses the residual radiation from immediately previous tests requested and approved for examinations by other traditional PET/CT commercially installed devices in hospitals. Subsequent tests for a screening study will require administering a dose of FDG (or any new radioisotope considered more suitable to signal to the physician the start of the development of a tumor) 1/30 of the 10 mCi used in current PET examinations, bringing the radiation dose to a level lower than the 1 mSv recommended by the safe ICRP for screening examinations.

The sequence of the tests on the new 3D-CBS device will be:

1. on phantoms to measure its efficiency, sensitivity, spatial resolution, etc.;
2. on patients (who underwent examination by traditional PET/CT) using the residual radiation of the radioisotope administered for that exam and quantitatively comparing the results relative to minimum abnormal metabolism - or other abnormal biological processes - in any area of the body acquired by the 3D-CBS with those acquired by the traditional PET/CT;
3. a study will be organized and conducted on a sample of asymptomatic high-risk patients following the procedure that has been used in the past for CT screening study. However, in this case, the total amount of radiation that the patient will receive from CT and the PET tracer should be lower than 1 mSv in order to comply with ICRP regulations.

Because the efficiency of the 3D-CBS is over 400 times that of the over 5,000 PET and PET/CT installed in hospitals around the world, it is expected that besides lowering the cost and providing more accurate information to the physician and to the patient, **the role of PET will be changed** from confirming the presence of an existing tumor (detected in most cases with other procedures, at an advanced stage) to that of benefitting asymptomatic patients and cancer survivors with early detection of the minimum abnormal metabolism (or other abnormal biological processes), that will offer a much higher chance for effectively curing their cancer and to be statistically among those with a 90% to 98% survival rate.

9. Rationale on how this innovations will reduce health care costs while saving more lives

The U.S. alone in 2003 spent $64.2 billion [7] mainly on drugs for treating cancer at an advanced stage (this expenditure increased in 2008 to $93.2 billion). Even with a much reduced budget for early detection, a better result in number of lives saved from premature death is guaranteed. When early detection is achieved, drug use drops and the cost for post-surgical treatment decreases because it is needed for a shorter period of time, in particular when the problem is solved mainly by the removal of early stage cancer with surgery.

A higher return in lives saved is supported by the following:

- **Efficacy of early detection:** Experimental data [31] show that when cancer is diagnosed at an early stage it is curable and life is saved in 90% to 98% of the cases ("Early-stage ovarian cancer is more than 90% curable; late stage is 75% deadly" [32])
- **Approved screening based on the measurement of tissue density which has low efficacy:** Despite the fact that cancer grows without always showing a change in tissue density, there is widespread screening with techniques such as mammogram which are based on measuring differences in tissue density
- **Higher efficacy obtained from measurements of metabolism** (or other abnormal biological processes) **compared to to measurements of tissue density:** Knowing that there is a better chance to detect cancer by a change in a normal biological process than a change in tissue density or other signals, "safe radiation dose" PET should be preferred over mammogram, CT, etc.
- **Validation by results obtained by a third party (Siemens) of the author's discovery made a decade ago - the possibility to increase efficiency of current PET by 400 times by improving the electronics and other sections of PET.** Third party validation of the author's

discovery confirms the claim that current PET efficiency can be increased by 400 times by extending the FOV and improving other sections of PET.

- **Certainty of obtaining at least 33% efficacy from screening with highly reliable and enormously more efficient technology.** A conservative estimate of 33% lives saved using this technology is compared with a lower percentage of cancer detected at an early stage by other techniques which are considerably less efficacious in early detection such as those which measurement of tissue density (e.g. mammography). From a given sample, the new technology will detect far more patients with early stage cancer that existing technologies. Since we know from experimental data that early detection results in 90-98% of lives saved regardless of method of early detection, it is obvious that more lives will be saved per sample tested using **the new 3D-CBS device**, which is much superior in technology (based on measurements at the molecular level rather than density) and with an efficiency 400 times superior compared to current PET. Thus, it **offers far greater advantages compared to the results in lives saved obtained during the past half century.**

National Cancer Institute (NCI) claims a reduction in cancer death of 2% per year (although this result is likely mainly due to smoking cessation or diet change, and a very small percentage due to research results).

However, when analyzing data obtained from the U.S. Census and U.S. CDC, and National Vital Statistics reported, it shows that from 2000 to 2003 the reduction ranges from 0.5% to 1.04% (see [19]). Even if 6,000 additional lives saved every year are included, considering the annual expenditures for cancer treatment of $64 billion for the year 2003 [7], the cost for each additional life saved is approximately $10.5 million ($64 billion/6,000. See details in Section 10, Table I of [29]).

Having established that the cost per each additional life saved has been approximately $10.5 million per person, one can compare that with the author's innovative solution targeted to early cancer detection, making it possible to reduce such expense by approximately 40 times.

The claimed health care cost reduction for cancer is supported by the following:

1. **Conservative estimate of the percentage of cancer death reduction through early detection:** Although experimental data show that early detection saves life in 90% to 98% of detected cases [31], in order to have good certainty that goals will be reached, only a conservative estimate of 33% reduction in cancer rate for a given population is assumed through screening with a technology that is 400 times more efficient than current 5,000 PET devices.

2. **Cancer death rate for the age group 50-75:** Statistical data show an annual percentage for cancer death rate of 0.5% in the age group 50-75 [4].
3. **Number of annual examinations required to achieve the same 6,000 lives saved result based on mortality rates (item 2) and estimate of lives saved currently in the U.S. (item 1):** In order to save the same 6,000 lives through early detection as accomplished now using current technology, it is necessary to examine about 3,640,000 people annually. [0.5% * 3,640,000 = 18,200; 18,200 * 33% = ~ 6,000]
4. **Cost to examine 3,640,000 people:** Because the cost of the examination performed with the author's innovative 3D-CBS technology is $400, to examine 3,640,000 people will cost $1.5 billion (plus the cost of surgery and post-surgical procedures). [$400 * 3,640,000 = ~$1.5 billion]
5. **Cost for each life saved:** Dividing the total cost of $1.5 billion by life saved, the cost per life saved is only $0.25 million (plus the cost of surgery and post-surgical procedures) using this new technology. [$1.5 billion / 6,000 = $.25 million]
6. **Possibility to save over 100,000 additional lives per year at a cost less than half compared to the current annual expense for cancer treatment:** With the author's discovery it is possible to greatly surpass the current limit of saving only 6,000 lives using current technology. By screening a larger sample of 60,000,000 people, it will be possible to save an additional 100,000 lives per year from premature cancer death at a cost of $24 billion (plus the cost of surgery and post-surgical procedures).

Of great impact will be the fourth and fifth achievement in the fight against cancer started ten years ago by the author. Most astonishing is the fourth achievement that can be reached for only $0.25 million (plus the cost of surgery and post-surgical procedures). Because currently the cost for each additional life saved is approximately $10.5 million, the cost enabled by this new discovery will be only one/fortieth (1/40) the current cost.

The fifth achievement deals with the possibility to save not only 6,000 people annually, but over 100,000 at a cost of $24 billion. That is still nine times less than the current annual cost for cancer to the U.S. of $228 billion [7]. Furthermore, there is an additional gain to the economy from people age 50-75 brought back to productivity instead of incurring high expenses for treatment of late stage cancer.

10. Measuring Results

Annual 3D-CBS examination will be performed on a representative sample of 10,000 people age 50-75, selected from a population in a location with a constant cancer death rate of 50 deaths per year recorded over the previous 20 years.

The examination should be safe for the patient requiring administration of a total radiation dose of 1 mSv, complying with ICRP regulations for screening, as for example has been done in the past for CT screening studies for cancer.

Results will be measured in terms of cost/benefits similar to other reports (for example the study made in Japan when in 2005, 50,000 people underwent PET screening in 46 hospitals [43]). Results should be published. Any reduction from the steady 50 deaths per year recorded during the previous 20 years will show success of the project.

Once the target of at least 33% premature cancer death reduction is achieved after 6 years, the project should be strongly supported and expanded with large investments.

11. Conclusions

These accurate measurements provided by the 3D-CBS innovative technology allow extraction of a maximum amount of useful information from each photon emitted, providing the **highest possible spatial resolution** and **highest sensitivity** using any type of crystal one chooses. This allows **precise pinpointing of the tumor** (as permitted by the intrinsic limitation of the radioisotope) at its **earliest possible stage**.

Higher efficiency and accuracy of 3D-CBS technology greatly **improves sensitivity and specificity** and reduces false positives and false negatives.

This innovative 3D-CBS technology passed several international scientific reviews extended to world participation in real-time via webcast (2003 in Dallas [27], 2008 in Rome [44]), and was presented recently by the author during over 100 hours presentation/discussion (most are available on video) with professionals at hospitals, universities, research centers (including Nobel Laureates at Erice on August 23, 2008 [30] and at CERN, via web EVO meeting on August 26 2008), to decision makers and citizens at city halls, province meetings with government representatives, cancer organizations, etc.

No professional has provided any valid criticism supported by scientific arguments to invalidate the author’s claims. 50,000 scientists affiliated with CERN recently **received the author’s key explanation [45] of the fundamental innovation** that had been misinterpreted by a reviewer, sent by cancer patient representatives. No one sustained the reviewer's misinterpretation, nor provided additional objections to invalidate the author's claims.

The anonymous reviewer's misinterpretations were clarified for him at a seminar/discussion by the author on September 24, 2009 at Brookhaven National Laboratory (BNL). Once again, **in a face-to-face discussion, the author was able to overcome a scientist's misinterpretation** which could have lead to a recommendation not to fund the author's innovations. In fact, as **witnessed on the video, scientists at BNL expressed their opinion that the project should be funded [44].**

On September 30, 2009, a forum was held in Pavia with participation of the President of the Association of Medical Physics in Italy and a U.S. scientist via webcast. On that occasion the author proved that the direction of research in the field is incorrect by pointing out that in the article by the Presidents of Medical Physics and Nuclear Medicine [46], which references 184 papers, and describes the traditional PET technology with the limitations in efficiency and cost-effectiveness. For example the attempt to increase PET FOV to 2 meters using RPC, low-efficiency detectors or a crystal thickness 4.5 mm instead of 25 mm, reduces detector sensitivity for a source point in the FOV to 20% from 95%. The author's innovative solution allows instead achieving high efficiency at any point of the FOV at low cost.

The rationale for the claimed reduction in premature cancer deaths of 33% (including tests to be performed to verify the claims) and the 40 times reduction in cost per life saved compared to current costs is described in [29].

Because the Japanese Health Care System in 2005 obtained better results by screening over 50,000 people in 46 hospitals using current inefficient PET/CT [43], compared to results obtained using other devices, surely they will obtain even better results using a device hundreds of times more efficient like 3D-CBS.

The reason why mammogram screening is approved by many countries is because it is claimed to save lives while using a safe radiation dose. PET molecular imaging is much more sensitive than mammography which measures tissue density. 3D-CBS is, in turn, over 400 times more efficient than current 5,000 PET and is suitable for screening examinations because it requires administration of a radiation dose equivalent to mammogram.

It begs the question, "how many more lives could be saved using the 3D-CBS technology?" And a second question: **"How long does it take to open the door to progress and fund the inventor to implement innovations**

that were recognized and approved as early as 1993 by Fermilab (and no one has invalidated any of the additional innovations in all this time)**?**

References

---

[1] The 38 industrialized countries (http://en.wikipedia.org/wiki/Developed_country) , listed as those "Very High Human Development" can be found at http://en.wikipedia.org/wiki/Human_Development_Index. Their population can be found at http://en.wikipedia.org/wiki/List_of_countries_by_population.

[2] National Institutes of Health estimates overall costs of cancer in 2008 at $228.1 billion. www.cancer.org/downloads/STT/500809web.pdf

[3] Alai, T., et al.: "The cost of cancer in Texas, 2007." Department of Preventive Medicine and Community Health University of Texas Medical Branch at Galveston. Texas Cancer Registry, Cancer Epidemiology and Surveillance Branch MC 1928, Texas Department of State Health Services, PO Box 149347, Austin, TX 78714-9347. www.crosettofoundation.org/uploads/327.pdf.

[4] National Vital Statistic Report NVSS-nchs showing the constant death rate of 300,000 deaths/year among the age group 50 to 75 years of age. www.cdc.gov/nchs/data/nvsr/nvsr53/nvsr53_15.pdf.

[5] Kolata, G.: "In Long Drive to Cure Cancer, Advances Have Been Elusive." The New York Times, April 24, 2009 http://query.nytimes.com/gst/fullpage.html?res=9A00EFDD143CF937A15757C0A96F9C8B63&sec=&spon=&pagewanted=all

[6] National Cancer Institute. Seethe cost of cancer in the U.S. in 1963 http://www.cancer.gov/aboutnci/servingpeople/costofcancer.

[7] National Cancer Institute. See the cost of cancer in the U.S. from 1960 to 2008 at www.crosettofoundation.org/uploads/329.pdf

[8] Peoples, J.: Letter from the Director of the Supercollider (also Director of FERMIlab) to the author, transmitting to him the "Patent Award check" with encouragements to continue his innovative activity to the benefit of mankind. http://www.crosettofoundation.com/uploads/174.pdf

[9] Crosetto D., "3D-Flow Processor for Calorimeter Triggers". Computing in High Energy Physics '92. Annecy, France. 21-25 September 1992. CERN-92-07. pp. 803-806.

[10] Crosetto D., "Programmable level-1 trigger for calorimeter." Calorimetry in High Energy Physics. Corpus Christy, Texas, September 29 – October 2, 1992. World Scientific. pp. 553-566.

[11] Crosetto, D.: "3D-Flow Processor for a Programmable Level-1 Trigger," SSCL-Preprint-164, Nuclear Science Symposium (NSS), Medical Imaging Conference (MIC), Orlando, Florida, October 25-31. 1992

[12] Crosetto, D. "A Fast cluster finding system for future HEP experiments. 1992. Published in Nucl.Instrum.Meth.A311:49-56,1992.

[13] Crosetto, D.: "A modular parallel processing system for trigger decision and DAQ in HEP experiments," Nuclear Instruments and Methods in Physics Research, A315, (1992), 487-490.

[14] Crosetto, D.: "General Programmable Level-1 Trigger with 3D-Flow Assembly System for Calorimeters of Different Sizes and Event Rates. SSCL-607, Dec. 1992. Submitted to Nuclear Instruments and Methods in Physics Research.

[15] Lefman, W.C., et al. GEM technical design report. By GEM Collaboration. GEM-TN-93-262, SSCL-SR-1219, Jul 31, 1993. 628pp. This version includes corrections through 15 June 1993.

[16] Crosetto, D.: "Massively Parallel-Processing System with 3D-Flow Processors." Published by IEEE Computer Society. 0-81816-6322-7194, pp. 355-369. 1994

[17] Crosetto, D.: Ninth Conference on Real-Time Computer Applications in Nuclear, Particle, and Plasma Physics. MSU, East Lansing, MI, May 23-26, 1995. IEEE Transactions in Nuclear Science, Feb. 1996.

[18] Amato, S. et al.: LHCb technical proposal. By LHCb Collaboration. CERN-LHCC-98-04, CERN-LHCC-P-4, Feb 1998. 180pp

[19] Crosetto, D.: LHCb base-line level-0 trigger 3D-Flow implementation. Nuclear Instr. and Methods in Physics Research, Sec. A, vol. 436 (1999) pp. 341-385. Part 1 http://www.crosettofoundation.com/uploads/147.pdf Part 2 http://www.crosettofoundation.com/uploads/148.pdf

[20] Crosetto, D.: 400+ times improved PET efficiency for lower-dose radiation, low-cost cancer screening. ISBN 0-9702897-0-7. 2000. Available at Amazon.com

[21] Crosetto, D.: A modular VME or IBM PC based data acquisition system for multi-modality PET/CT scanners of different sizes and detector types. Presented at the IEEE Nuclear Science Symposium and Medical Imaging Conference, Lyon, France, 2000, IEEE-2000-563, Hhttp://www.3d-computing.com/pb/ieee2000-563.pdf.H

[22] Crosetto, D.: Real-time, programmable, digital signal-processing electronics for extracting the information from a detector module for multi-modality PET/SPECT/CT scanners. Presented at the IEEE Nuclear Science Symposium and Medical Imaging Conference, Lyon, France, 2000, IEEE-2000-567, Hhttp://3d-computing.com/pb/ieee2000-567.pdf

[23] Crosetto, D. Saving lives through early cancer detection: Breaking the current PET efficiency barrier with the 3D-CBS." 2001. Hwww.3d-computing.com/pb/3d-cbs.pdfH. Hhttp://www.crosettofoundation.com/uploads/100.pdfH

[24] Crosetto, D.: "Development of an Innovative Three-Dimensional Complete Body Screening Device - 3D-CBS" Book: Astroparticle, Particle and Space Physics, Detectors and Medical Physics Applications. Editor: World Scientific, 2004, pp. 350-359. Hhttp://www.crosettofoundation.com/uploads/103.pdfH

[25] Crosetto, D.: "The 3-D Complete Body Screening (3D-CBS) Features and Implementation" IEEE-NSS-MIC-2003. Conference Record. M7-129. www.3d-computing.com/pb/HIEEE2003_M7-129p.pdfH. Hhttp://www.crosettofoundation.com/uploads/107.pdf

[26] Crosetto, D.: "3D-Flow DAQ IBM PC board for Photon Detection in PET and PET/CT" IEEE-NSS-MIC-2003. Conference Record. M3-130. Hhttp://www.crosettofoundation.com/uploads/105.pdfH

[27] See Final Report of the committee who reviewed Crosetto's innovative technology at Hwww.3d-computing.com/pb/Review_rep.pdf.H Hhttp://www.crosettofoundation.com/uploads/101.pdfH

[28] Crosetto, D.: "Rethinking Positron Emission Technology for Early Cancer Detection" Book: Astroparticle, Particle and Space Physics, Detectors and Medical Physics Applications. Editor: World Scientific, 2006, pp. 692-696. http://www.crosettofoundation.com/uploads/112.pdf

[29] Crosetto, D.: "Ignored Discovery Now Proven Capable of Saving Millions of Lives from Premature Cancer Death Demands Rethinking the Direction of Research" Book: Astroparticle, Particle and Space Physics, Detectors and Medical Physics Applications. Editor: World Scientific, pp.624-639 - 2008. http://www.crosettofoundation.com/uploads/134.pdf

---

[30] Crosetto, D: “Logical Reasoning and Reasonable Answers Consistent with Declared Objectives for the Benefit of Mankind.” International Seminars on Planetary emergencies 40th Session, Erice, 19-24 August 2008. www.crosettofoundation.com/uploads/211.pdf

[31] Cancer incident and survival in United States recorded between 1960-2004, compiled by the Surveillance Epidemiology, and End Results (SEER), a program of the National Cancer Institute (NCI). www.crosettofoundation.org/uploads/233.pdf

[32] Leaf, C.,: “Why we’re losing the war on cancer” FORTUNE magazine, March 22, 2004, pp.76-94. www.crosettofoundation.org/uploads/229.pdf.

[33] Goatz, T.: “Why Early Detection Is the Best Way to Beat Cancer.” WIRED Magazine, December 22, 2008. www.crosettofoundation.org/uploads/231.pdf

[34] 3D-Flow basic invention: www.crosettofoundation.org/uploads/291.pdf

[35] 3D-Flow glossary: www.crosettofoundation.org/uploads/239.pdf

[36] Ellis, N. et all.: “A Calorimeter-Base Level-One Electromagnetic Cluster Trigger for LHC.” Computing in High Energy Physics ’92. Annecy, France. 21-25 September 1992. CERN-92-07. pp. 210-213.

[37] Ellis, N.: “Level-1 and Level-2 Triggering at LHC.” Calorimetry in High Energy Physics. Corpus Christy, Texas, September 29 – October 2, 1992. World Scientific. pp. 471-487.

[38] Guida, J.: “The DØ Calorimeter Trigger.” Calorimetry in High Energy Physics. Corpus Christy, Texas, September 29 – October 2, 1992. World Scientific. pp. 465-470

[39] Sullivan, W.G.: “SDC Calorimeter Trigger.” Calorimetry in High Energy Physics. Corpus Christy, Texas, September 29 – October 2, 1992. World Scientific. pp. 488-493.

[40]Testimonials and evaluations from experts in the field who have appreciated author’s innovations and scientific approaches, http://www.crosettofoundation.com/uploads/167.pdf

[41] See Siemens website http://www.medical.siemens.com stating in 2007 “electronics significantly [70%] improved…”

[42] See the 5 minutes movie explaining in simple terms with an analogy the first invention by the author in 1992 (see http://www.youtube.com/watch?v=O45IE5jwQXQ.)

[43] Minamimoto, R., et al.: “Performance profile of FDG-PET and PET/CT for cancer screening on the basis of a Japanese Nationwide Survey.” Ann Nucl Med. 2007 Nov;21(9):481-98. Epub 2007 Nov 26. http://www.ncbi.nlm.nih.gov/pubmed/18030580

[44] See website www.crosettofoundation.org

[45] Key innovation expl. http://www.crosettofoundation.com/uploads/324.pdf

[46] Pedroli, G. Salvo, pp. 26-68. www.crosettofoundation.org/uploads/288.pdf