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 - Facts & Figures - dimensions of the problem

In the 38 industrialized countries\(^1\), listed as those with “Very High Human Development” with a total population of 989 million, the total cost of cancer is $741 billion/year. This cost, calculated as the total cost of cancer\(^a\) in the U.S. in 2008 is $228.1 billion, divided by the population as of July 1\(^b\), 2008 of 304 million\(^c\), equals $750/per-capita annually. Despite such high costs, every year among this population of 989 million, cancer takes the highest toll of one million premature deaths per year just in the group 50-75 years of age, more than any other disease, war or calamity\(^d\). The $93.2 billion direct medical expenditures\(^e\) for cancer in the U.S. in 2008 is about 100 times those of 50 years before (in 1963 only $1.2 Billion\(^f\)), while the increase in cost of living was only 3 times. During the past 50 years reduction in cancer death has been recorde\(^g\) as a mere 5%, while for heart disease the reduction was 64%.

That the direction in cancer research needs to be changed to make it more efficacious is proven because the reduction is not much different in less developed countries that do not have a cost of $741 billion/year.

\(^a\) $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).
In 1993 a major scientific review of a breakthrough technology invented by the author, the basis for a substantial reduction in premature cancer deaths 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.), the most prestigious universities (Chicago, Michigan, Irvine, etc.) and leading industry (DEC). In one month in 1992, the innovation was presented at three international conferences in Europe and the U.S. and two of the author’s articles were published in peer reviewed scientific journal *Nuclear Instruments and Methods in Physics Research*. Surprisingly, 17 years after the invention was recognized and approved, and during the past 12 years when the author submitted proposals to implement ALL his inventions related to medical imaging for early cancer detection, no funds were awarded.

Had a mere 0.0002% of those $8 trillion cancer cost during the past 12 years been diverted to such an award, it would have resulted in over 33% reduction in premature cancer deaths instead of the 2% realized. (See details at: www.crosettofoundation.org/uploads/330.pdf)

2. What is Cancer, how is it manifested and how can it be defeated?

Cancer is a disease characterized by the mutation of normal body cells into cancerous cells whose main characteristic is out of control reproduction, and transported through the blood vessels to other distant tissues (metastasis).

Experimental data confirm that cancer diagnosed at an early stage, at the development of the very first cancerous cells, has 90% to 98% probability of resulting in a life saved. Development of cancerous cells can be associated with signals. Such signals are related to changes in: odor, temperature, tissue density, fluorescence, metabolism, perfusion, etc. Among all these signals, the ones most reliable and useful for early detection are those showing change in metabolism (up to 70 times higher in cancerous cells) and other biological processes at the molecular level, even before symptoms or morphological changes occur (e.g. change in tissue density that will be detected at a later stage by mammogram, X-rays, CT, MRI, Ultrasound, etc.).

3. Limits of current PET overcome by the 3D-CBS invention

Due to their low efficiency, the current over 5,000 Positron Emission Tomography (PET) devices cannot provide early detection because they capture and inaccurately measure only one signal out of 10,000 from the tumor markers. Current PET examinations are costly and require a radiation dose over ten times higher than the level recommended by ICRP as safe for screening.
The innovative 3D-CBS technology can capture and accurately measure 1 out of 25 signals from the tumor marker (400 times efficiency improvement) allowing achievement of true safe early detection cost effectively. 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 justification for the use of expensive treatments 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 the restart of activity in cancer survivors). It is this early detection that has been shown to save lives.

3.1. Basic invention of 1992 relative to the increase in efficiency

The basic invention in 1992 of the 3D-Flow parallel-processing system made possible execution of complex real-time algorithms for a time longer than the time interval between two consecutive input data with the capability of neighboring data correlation with no boundary. This provides the advantage to fully utilize all the radiation – nothing is lost. The solution is much more critical for Medical Imaging than for Particle Physics. In Particle Physics, inefficiency only causes a delay and higher cost in discovering new particles. Much more serious and damaging, inefficiency in Medical Imaging devices increases the cost for health care, and 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 to be able to reduce false positives and false negatives.

3.2. Additional inventions related to early cancer detection

Additional inventions published by the author since 2000 relate to the specific application of the innovation to medical imaging in the areas of physics, mechanics, geometry, data-flow, system architecture, electronics, coupling between detector and electronics, etc. These inventions allow for a simple system, although the detector length has been increased and more information is extracted using more economical crystals, with the result of providing at a reasonable cost a much more powerful system not previously envisioned. The optimized improvements are the right balance between the extension of the Field Of View (FOV), the cost of the crystals, a simplified detector assembly, and novel electronics at lower speed and greater economy. 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 comprehensive understanding of a single part, let alone an assessment of the synergy of the entire system.

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 early diagnosis of cancer and the reduction of “false positives” and “false negatives” at a lower examination cost. 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 (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.

The new concepts are proven by logical arguments in articles 7, 11, 12, 13, 15, by simulation (Sections 11, 12 of ref. 11, Appendix of ref. 15, Chapter 13 of ref. 12), by construction of the innovative parts in working hardware17 and by experimental results of third parties (i.e. Siemens25) confirming the author’s claims. These accurate measurements 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 Dallas19, 2008 in Rome26), 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 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 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.

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, 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 refs. 21, 23.

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, 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. 38 industrialized countries (http://en.wikipedia.org/wiki/Developed_country)
26. See website www.crosettofoundation.org