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Sviluppo di una SPECT Camera per lo studio di Radiofarmaci “intelligenti” su piccoli animali

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L'uso di radiofarmaci, tra le molteplici applicazioni delle radiazioni, trova completa giustificazione in campo medico. I **radiofarmaci** sono sostanze chimiche che, in quanto farmaci, hanno la proprietà di interagire specificatamente con il sistema biologico e che, contenendo nella loro struttura un atomo di un nuclide radioattivo **emittente gamma** (radiazione scarsamente assorbita dai tessuti biologici), consentono di seguirne il percorso biologico per mezzo di idonei rivelatori esterni. È così possibile costruire una serie di immagini, raccolte in tempi successivi, che individua la distribuzione del radiofarmaco nel corpo e ne evidenzia il progredire del metabolismo. In questo modo è possibile avere indicazioni, non solo morfologiche di organi e apparati, ma soprattutto informazioni sulla loro funzionalità.

L'informazione clinica che si ottiene dall'analisi delle **immagini scintigrafiche**, dipende sostanzialmente dalle proprietà biologiche che il radiofarmaco possiede una volta iniettato *in vivo*. Se il radiofarmaco ha inoltre la proprietà di fissarsi specificamente in cellule tumorali, esso può diventare anche **radioterapeutico**. Basta infatti utilizzare nella **"marcatura"** un radionuclide che emetta radiazioni adatte alla distruzione delle cellule tumorali (radiazioni corpuscolari a corto range nella materia biologica) perché il radiofarmaco affine ad esse, iniettato *in vivo*, trasporti l'agente terapeutico specificamente nella zona di azione.

Experimental set-up

A new experimental set-up is under development. It makes use of two position-sensitive photomultiplier tube (PSPMT) Hamamatsu H8500 (***Fig.1***). The sensitive surface of this device has dimensions of 52×52 mm^2 and holds 8×8 anodes with small dead space. The photocathode is made of bialkaly and the 12-stage multiplier furnishes a typical gain of 10^6 at -1100V of anode voltage.

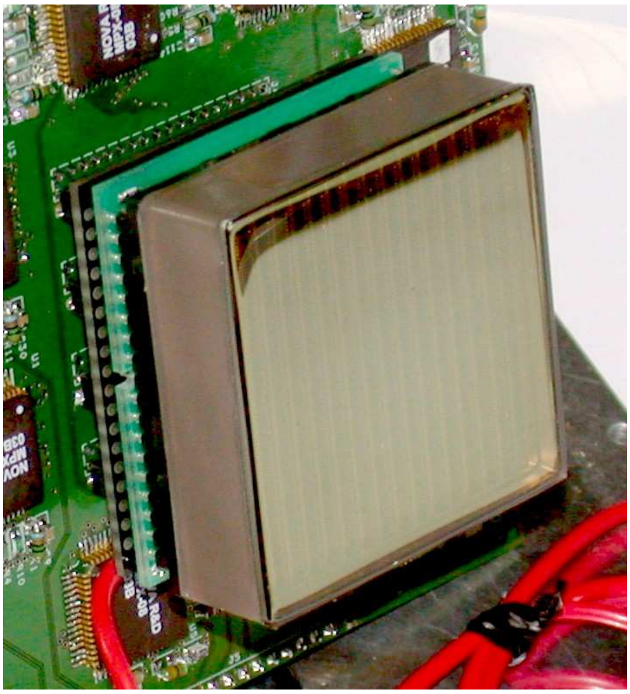


Fig.1: *A view of the H8500 PSPMT.*

The two PSPMT – each one fitted on its electronic board – will be coupled with a $LaBr_3$:Ce scintillator slab and with a lead collimator (see **Fig.2**) and housed inside a lead shield.

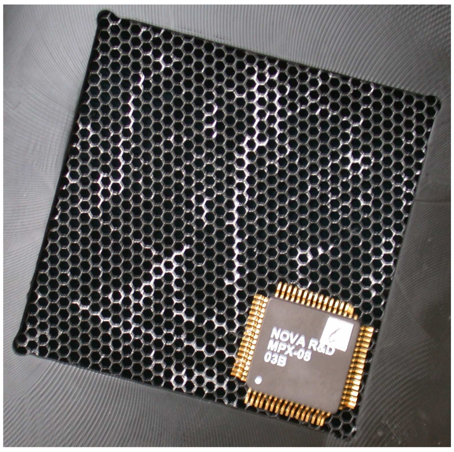


Fig.2: *A view of the multi-hole collimator coupled with the H8500 PSPMT and the scintillator slab. Hexagonal holes have diameters of 1.5mm or 1.0mm. An MPX-08 chip is also shown.*

The detectors will be positioned at an angle of 90° one for respect to the other so they can see a mouse placed inside the triangular section shielding (see ***Fig.3*** and ***Fig.4***).

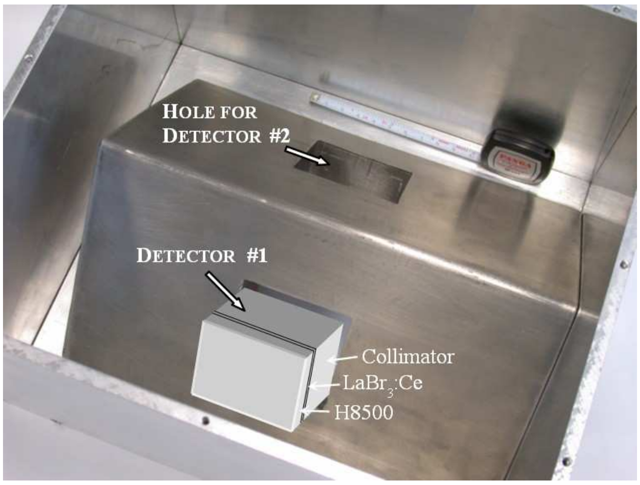


Fig.3: *A top view of the triangular section lead housing with the two holes in which detectors will be embedded. The mouse enters on the bottom right and the detection system will rotate around it.*

Fig.4: *Bottom view of the lead housing. This is the mouse hole. Detectors face at 90°.*

All the detection system, constituted from the two H8500 PSPMT each one with its LaBr$_3$:Ce scintillator slab and multi-hole collimator, will be mounted on a motorized rotating stage (see **Fig.5**) to perform a tomographic reconstruction of the tracer inside the mouse under examination.

A brief explanation of the components selected and the choices made during this development follows.

The H8500 FLAT PANEL

This compact 64 anode PSPMT is ideal to realize a detector wall with minimized dead space on the boundaries. Here only two H8500 are coupling to perform the mouse tomography.

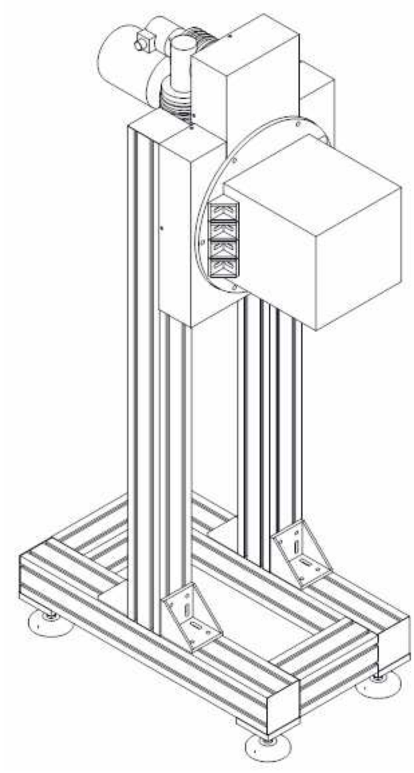
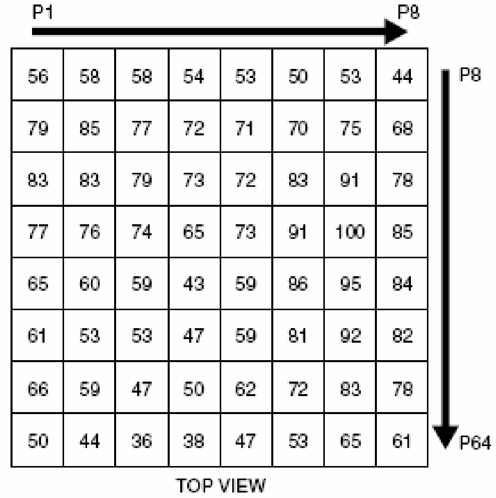


Fig.5: *The rotating stage is under construction. The box you will see in front of them represents the external housing of the detection system.*

In Fig.6 the anode uniformity of the H8500 is shown. The best photocathode sensitivity is in the range 300÷500nm. The typical dark current is of 0.5nA per anode. The transit time of the electrons is of about 6ns.



56	58	58	54	53	50	53	44
79	85	77	72	71	70	75	68
83	83	79	73	72	83	91	78
77	76	74	65	73	91	100	85
65	60	59	43	59	86	95	84
61	53	53	47	59	81	92	82
66	59	47	50	62	72	83	78
50	44	36	38	47	53	65	61

Fig.6: *H8500 typical anode uniformity (W lamp at 2856K).*

The LABR$_3$:CE scintillator

The new scintillation crystal LaBr3:Ce shows an impressive light output and energy resolution (see **Fig.7** and **Table 1**). In addition the very short scintillation decay time could contribute in building new PET based on time of flight due to coincidence resolution time as low as 250ps [1].

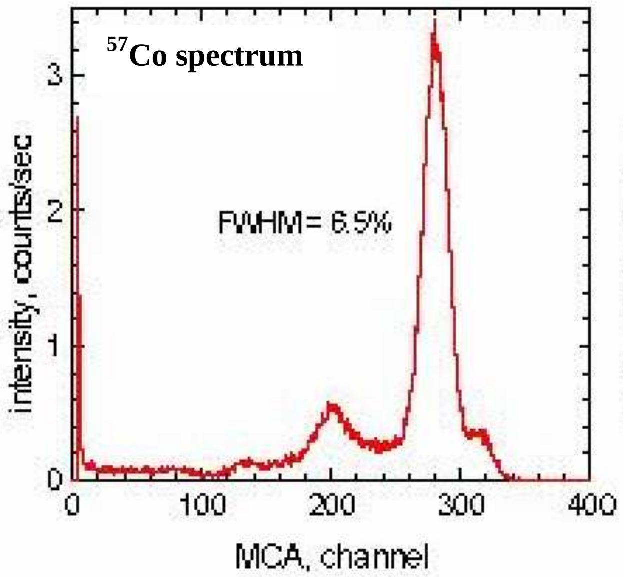


Fig.7: *The energy resolution of LaBr$_3$:Ce is very high in comparison with other scintillator materials.*

Properties	**NaI(Tl)**	**LaBr$_3$:Ce**
Light yeld (photons/keV)	38	49
Light output (% NaI(Tl) with bialkaly PMT)	100	70÷90
Wavelenght of maximum emission	415	350
1/e decay time	250	28
Energy resolution (137Cs)	7%	3.5%
Refractive index	1.85	1.9
Density	3.67	3.79

Table 1: *summary of the LaBr$_3$:Ce properties in comparison with NaI(Tl) scintillato (source: Saint-Gobain)r.*

The MPX-08 CHIP

The MPX-08 integrated circuit (**Fig.2**) is an eight channel charge integrating analog data acquisition system, suitable for measuring charges in the range from several fC to over 10 pC. It has been developed primarily for use with photomultiplier tubes and similar devices in applications involving discrete charge pulse events. The signal range is typically from <1 photoelectron up to >50 photoelectrons, assuming a nominal PMT gain of 10^6. The MPX-08 is particularly well suited to minimize power in large pulse-mode detector systems.

A block diagram of the MPX-08 is shown in **Fig.9**. Each channel includes a charge integrating input amplifier with variable gain controlled from a binary word and two discriminators, the “lower level discriminator” (LLD) and the “upper level discriminator” (ULD). The charge integrating amplifier outputs connect to transparent track/hold buffers, all controlled by a common TRACK control signal. Readout of the latches and track/hold buffers is under the control of address input bits ADDR3÷ADDR0. Readout of the buffer stage can proceed independently from the operation of the input amplifier and discriminator stage.

The MPX-08 requires a power supply of 3.3V with a dissipation of 4.39mW.

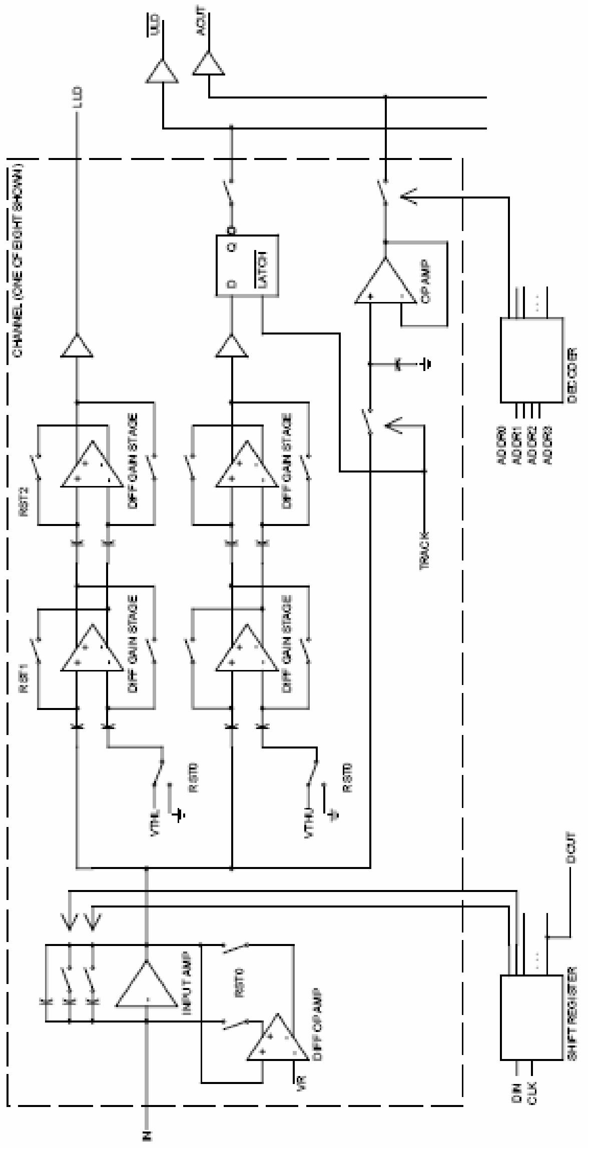


Fig.9: *Block diagram of MPX-08 ASIC.*

CONDITIONING AND ACQUISITION ELECTRONICS

The use of MX-08 ASIC as the front-end electronics require some logic circuitry: 1) to set the charge sensitive preamplifier gain, 2) to set the integration time – as a function of the scintillator type and its eventual afterglow time, 3) to discharge feedback capacitor after the pulse generation, 4) to decode the serial output of each MPX-08, 5) to address the eight ICs and 6) to generate the START CONVERSION pulses and the logic sequence to control the PCI-6025 acquisition board. In **Fig.10** one can see a simplified block diagram of the connections for one of the H8500 PSPMT.

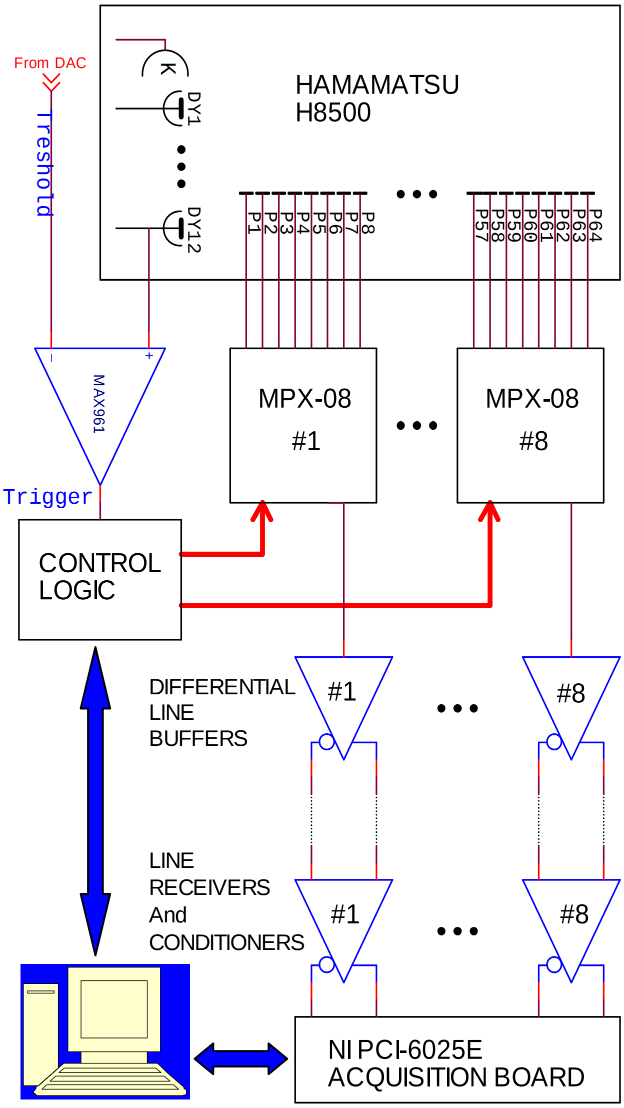


Fig.10: *Block diagram of the electronics developed to acquire the 64 signals from one H8500 PSPMP. The PCI-6025 board can acquire 16 differential channels, so the same board was used for both the PSPMT.*

The trigger signal comes from the 12th dynode of any H8500 and starts the acquisition of all the 64 signals. Output signals are converted in differential mode and transmitted to a receiver-conditioning stage that allows to correct differences in gain and offset – to perform a row equalization accounting the anode non uniformity and the MPX-08 offset/gain tolerance – and then converted by the National Instruments PCI-6025 board. Any H8500 unit can acquire about 6000 events per second. In **Fig.11** one of the prototype boards is shown.

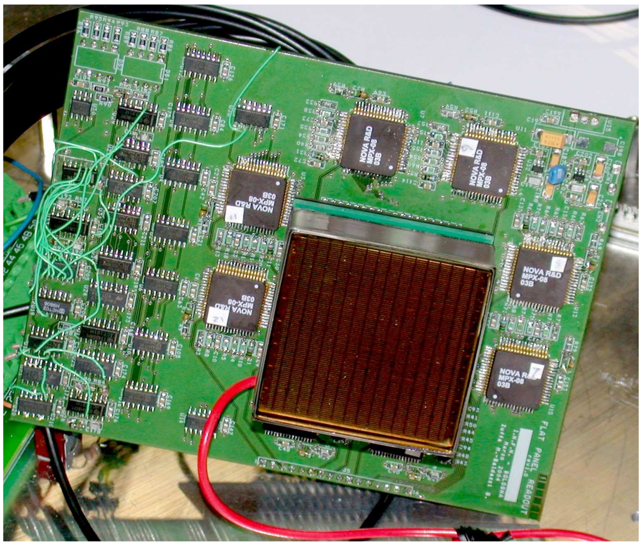


Fig.11: *A prototype of the circuit board realized and tested. The H8500 PSPMT is surrounded by eight MPX-08 ASIC. In this board there is also the triggering circuitry and the control logic. The line buffers are housed on a piggy-back smaller board.*

In Fig.12 a raw spectrum is shown. Obtained with a source of ^{57}Co and the LaBr$_3$:Ce scintillator slab, the spectrum is the sum of all 64 channels before of its fine equalization that will be performed via software.

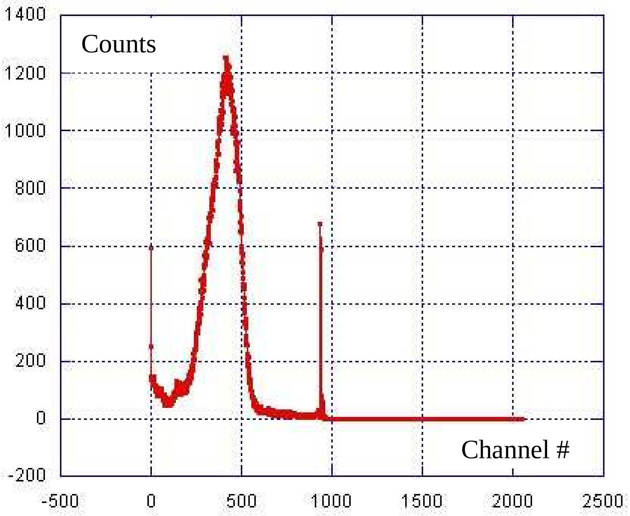


Fig.12: *Raw spectrum of ^{57}Co obtained with the prototype electronics.*

Future developments

The tomographic system based on two H8500 PSPMT and $LaBr_3$:Ce scintillator will be soon completed. Therefore a new fascinating perspective presents: Hamamatsu have recently developed a new PSPMT, the H9500, with the same dimensions of the H8500 but with 256 anodes and pixels of 3×3mm^2. This is the state-of-art and probably the ultimate limit of this technology.
The study to realize the electronics to read and acquire data from this new H9500 PSPMT have been started. A 32 channels low-noise/low power high dynamic range charge sensitive preamplifier-shaper circuit, with simultaneous sample and hold, multiplexed analogue readout and calibration facilities will be employed. This circuit offers also a full parallel readout of all 32 channels (**Fig.13**).

ideas **VA32 HDR11**

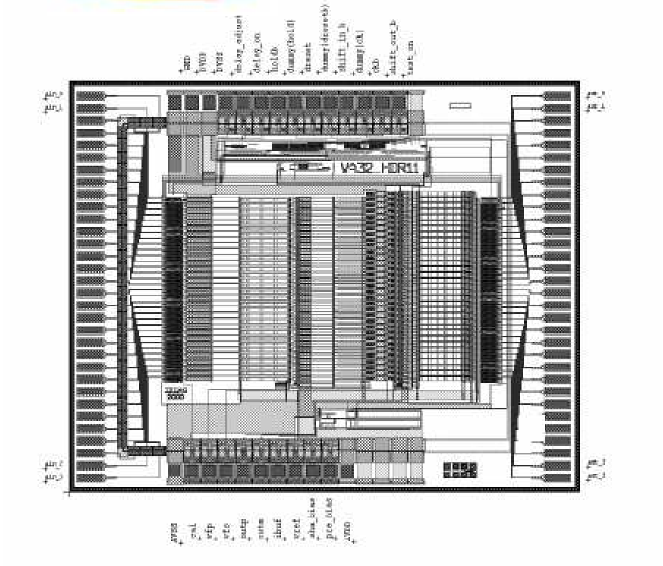


Fig.13: *The Ideas VA32 32 channels bore chip. It will be bonded inside an "open cavity", a molded package with external surface mounting reophores. The electronics will be built in a "vertical arrangement" to obtain a compact detection stage compatible to the realization of detectors wall.*

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For more information see:
http://www.bo.infn.it/scintirad/progetto.htm