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BIOMEDICAL APPLICATIONS OF MWPC's FOR DIGITAL IMAGING
OF SOFT β^- EMITTERS

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ABSTRACT

We have built an experimental facility equipped with MultiWire Proportional Chambers and a PDP 11/23 mini-computer for the digital imaging of two-dimensional ^3H distributions in biological and medical applications.

A spatial resolution of ~ 1.5 mm (FWHM), a sensitivity of 10^{-1} Bq/cm², and an efficiency of $\sim 10\%$ with an uniformity of 4% have been measured with a MWPC working at atmospheric pressure with 2 mm anode pitch and cathode coupled delay line read-out. A second chamber with 1 mm anode pitch at 45° with respect to the cathode wires has been operated at 2 atm. In this case a spatial resolution of ~ 800 μm (FWHM) for ^3H sources has been measured along both directions.

The image obtained in biological and medical applications are presented, namely:
i) identification of human clones with defective repair of UV-induced damage; ii) study of regional carbohydrate consumption in myocardial tissue.

1. - INTRODUCTION

In previous papers^(1, 2) we have shown how it is possible to use a MultiWire Proportional Chamber for the imaging of ^{14}C -labelled living human cells. A spatial resolution of 4-4.5 mm (FWHM) was reported with a detection efficiency of $\sim 20\%$ ⁽²⁾.

A crucial problem for the imaging of distributions of β^- activity with gaseous detectors is connected with the range of the β^- rays inside the detector volume. In this respect the use of ^3H as a labelling agent should be favored because of its shorter range ($E_{\text{MAX}} = 18 \text{ keV}$; maximum range $\approx 5.9 \times 10^{-3} \text{ g/cm}^2 \approx 3 \text{ mm}$ in Argon S. T. P.). Tritium is also cheaper than ^{14}C ; its specific activity can be a thousand-fold higher and it is easier to handle. However, the ^3H imaging with the film autoradiography technique presents severe limitations for the low sensitivity of the film to low energy β^- rays; furthermore, quantitative information can be obtained with difficulty because of the non linear response of the film to the energy deposited by the β^- particles, and of the intrinsic variability of the photographic process. The use of electronic gaseous detectors, on the other hand, requires a specially designed device with practically no absorbing material between the sample to be imaged and the active volume of the detector.

For this purpose we have built two windowless MWPC's for the imaging of ^3H -labelled samples: the first one operates at atmospheric pressure, and the second one can be pressurized up to 4 atm. In this paper we present their performance and discuss their use in biological and medical applications.

2. - THE MWPC'S AND THE READ-OUT SYSTEM

The MWPC's have a typical active area of 625 cm^2 with an anode-cathode gap of 4.0 mm. Gold-tungsten wires have been used for the anode plane ($20 \mu\text{m}$ diameter) and copper-beryllium wires for the cathode planes ($100 \mu\text{m}$ diameter). Standard Ar/Isobutane and Ar/ CO_2 gas mixtures have been used.

In order to be able to detect the ^3H β^- rays the chamber must act as a "windowless" detector. With the chamber operating at atmospheric pressure and in gas flow condition, this is achieved by using an easily removable top-frame. Only a few minutes are necessary before the working conditions of the chamber are restored after the opening to insert the sample. In the case of the pressurized chamber, both the MWPC and the sample are placed inside a stainless steel box which is then pressurized. In both cases the sample is positioned inside the chamber at $\sim 200 \mu\text{m}$ from the cathode plane.

We have adopted a cathode-coupled delay line read-out system with the anode signal only used as a gate. The delay line and its characteristics have been fully described elsewhere⁽¹⁾: its measured specific delay is $64.2 \pm 0.1 \text{ ns/cm}$. A schematic drawing of the electronics and of the read-out system is shown in Fig. 1. The pick-up and the processing of the signals are obtained by means of low noise charge sensitive pre-amplifiers which constitute the "cold" termination of the delay line. The processed signals from the two ends of each delay line are the START and the STOP of two Time to Amplitude

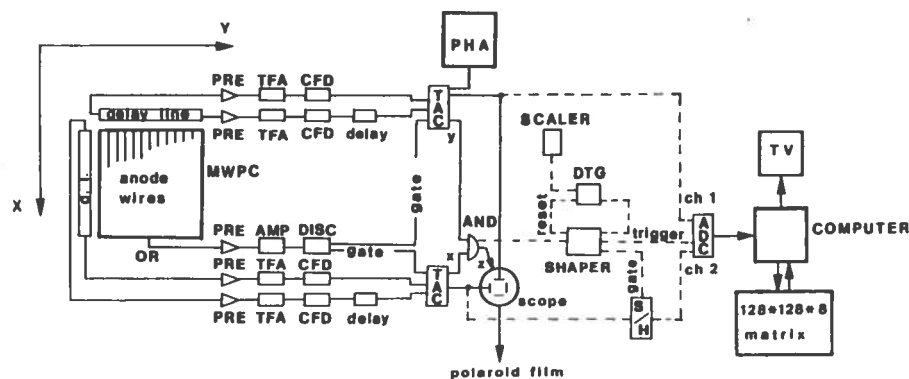


FIG. 1 - Schematic drawing of the electronics and of the read-out system: analog (—) and digital (----) system. TFA = Timing Filter Amplifier; CFD = Constant Fraction Discriminator; DTG = Dead Time Generator; S/H = Sample and Hold unit.

Converters (TAC Ortec 467). Two flexible, parallel, data acquisition systems - one analog and one digital - have been implemented. The output from each TAC drives the x (y) deflection plate of an oscilloscope. The z-axis is intensified by the AND of the two TAC's. A Polaroid film is used as a permanent storage of the obtained analog information. This system is well suited for trouble shooting as well as for control and immediate feedback on the experiment. However, because of the narrow range of linearity of the Polaroid film and its poor grey level characteristics, a digital system is used for off-line data reduction and analysis. The output signals from the two TAC's are digitized by means of a 12 bit Analog to Digital Converter (ADC, DEC-MINC-11). The digital information, proportional to the x and y coordinates of the detected event, is stored via a mini-computer (PDP 11/23) onto a permanent magnetic memory (floppy disk), and subsequently processed and displayed onto a specialized image processing device (Tesak VDC-501).

3. - THE PERFORMANCE OF THE MWPC AT ATMOSPHERIC PRESSURE

The first MWPC operates at atmospheric pressure. It has a 2 mm anode wire pitch. An energy resolution of 14% FWHM has been obtained for 5.9 keV X-rays, with a noise level of 10^{-2} Hz/cm². A spatial resolution of 400 ± 50 μ m has been measured using a ⁵⁵Fe source with a linearity of < 0.5%.

The resolving power of the system, i. e. the capability of identifying individual spots of β^- radioactivity, has been measured⁽³⁾ to be ~ 1.5 mm along the anode wire. The resolution in the direction orthogonal to the anode wires is somewhat ($\sim 30\%$) worse due to the finite sampling along that direction (2 mm). The uniformity of response to a two-dimensional activity has been checked by moving a ³H disk source (5 cm²) at many (~ 40)

FIG. 2 - The resolution ^3H phantom consisting of equally spaced parallel lines of 3, 2 and 1 mm : a) analogue reconstruction at 1 atm ; b) at 2 atm (Raw data).

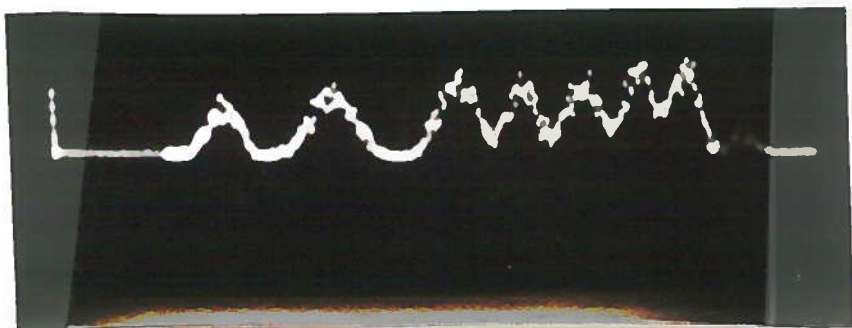
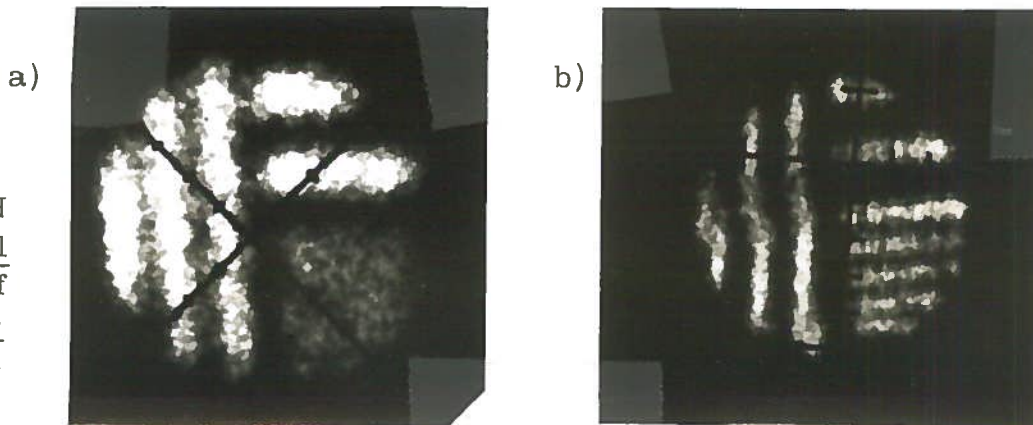


FIG. 3 - Line profile of the ^3H phantom across the 3 and 1 mm parallel lines.

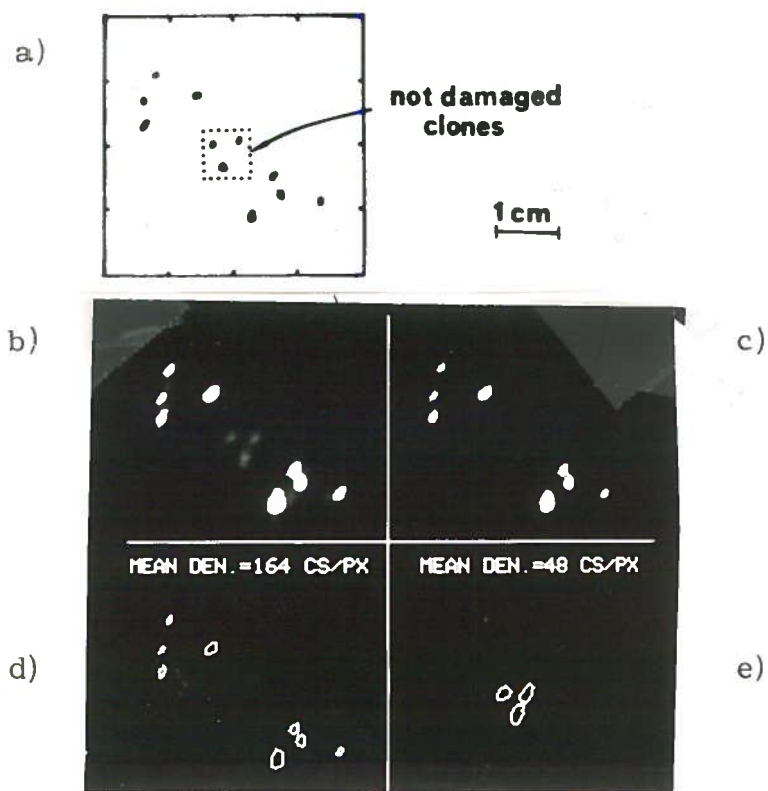


FIG. 4 - Typical imaging experiment with human cells : a) a sketch of the pattern of ^3H -labelled clones ; b) the original image ; c) after background subtraction ; d) the contours of the clones at 30% threshold ; e) the contour of the not damaged clones, which simulate the expected background activity in non repairing cells.

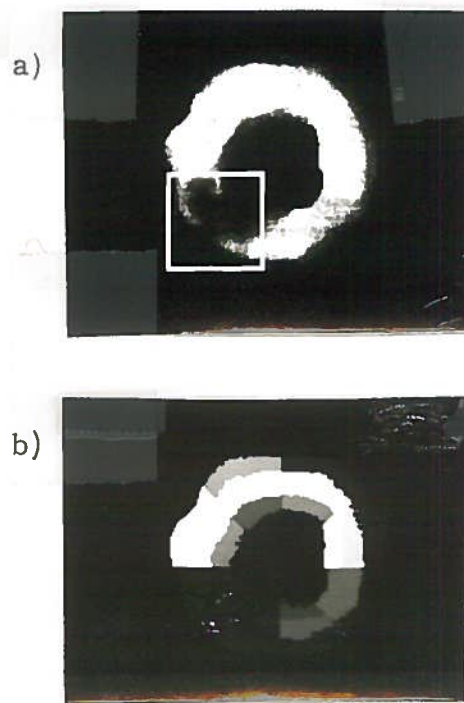


FIG. 5 - Left ventricle image of the heart of a dog in which an ischemic condition was artificially induced : a) raw data ; b) after regional computer analysis. A cold area is well evident inside the white box.

With the MWPC all colonies with absent or low incorporation of ^3H -thymidine can be precisely located within a population of normally labelled colonies. In order to test the ability of the MWPC to discriminate between mutant and normal colonies, several reconstruction experiments have been performed^(3,4). Fig. 4 shows a typical experiment: Fig. 4a is a sketch of the original colonies distribution, where the non UV-damaged clones simulates the non repairing cell colonies. Fig. 4b-e shows the processed image of the colonies as obtained in 20 min of data taking with the MWPC operating at 1 atm. The activity of the cells is 15 Bq/clone.

A second series of experiments was related to the use of the MWPC for the study of the regional carbohydrate consumption in myocardial tissue⁽⁵⁾ with a deposit tracer of glucose metabolism (^3H -deoxyglucose). Typically, 8×10^7 Bq of ^3H -DG is injected intravenous to a dog. After two hours the animal is killed with an overdose of anaesthetic and the heart is excised. Ultra thin heart slices of about $40 \mu\text{m}$ are then obtained by means of a microtome. Some of these slices are placed inside the MWPC for the β^- radioactivity measurement. Fig. 5 shows an example of the ^3H -DG distribution in a micro slice of a dog in which an ischemic condition was artificially produced. Fig. 5a shows the raw image and Fig. 5b the image after the computerized regional analysis has been performed⁽⁶⁾.

6. - CONCLUSION

We have shown that the MWPC's we have built are very useful detectors for digital imaging of two-dimensional distributions of soft β^- emitters. Compared with the conventional film autoradiography technique, they have a much higher sensitivity, especially with ^3H -labelled compounds. Furthermore, the use of the MWPC provides quantitative information about the two-dimensional distribution in a very short time, and digital images are obtained directly, without the time consuming procedure of decoding from an analog picture.

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