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BIOMEDICAL APPLICATIONS OF MWPCs FOR DIGITAL IMAGING OF SOFT β^- EMITTERS

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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 ^{3}H distributions in biological and medical applications.

A spatial resolution of ~ 1.5 mm (fwhm), a sensitivity of 10^{-1} Bq/cm^2, and an efficiency of ~ 10% with a unifomity of 4% have been measured with a MWPC working at atmosheric 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 ^{3}H sources has been measured along both directions.

The images obtained in biological and medical applications are presented, namely: (1) identification of human clones with defective repair of UV-induced damage, (2) 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 ~ 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 ^{3}H as a labelling agent should be favored because of its shorter range (E_{max} = 18 keV; maximum range $\simeq 5.9 \times 10^{-3}$g/cm^2 $\simeq$ 3 mm in argon STP). Tritium is also cheaper than ^{14}C; its specific activity can be a thousand-fold higher and it is easier to handle. However, ^{3}H 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 MWPCs for the imaging of ^{3}H-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 MWPCs and the read-out system

The MWPCs 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 μm diameter) and copper–beryllium wires for the cathode planes (100 μm diameter). Standard Ar/isobutane and Ar/CO_2 gas mixtures have been used.

In order to be able to detect the ^{3}H β^- rays the chamber must act as a "windowless" detector. With the chamber operating at atmosheric 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 an aluminum box which is then pressurized. In both cases the sample is positioned inside the chamber at ~ 200 μm 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 ± 0.1 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 converters (TAC Ortec 467). Two flexible,

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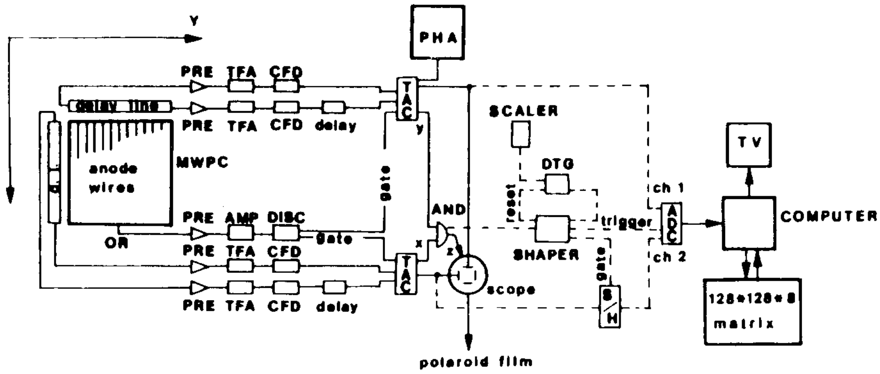

Fig. 1. Schematic drawing of the electronics and of the read-out system: analog (—), and digital (---) system. TFA = timing filter amplifier; CFD = constant fraction discriminator; DGT = dead time generator; S/H = sample and hold unit.

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 TACs. 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 TACs 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 (PDP11/23) 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/cm^2. A spatial resolution of 400 ± 50 μm has been measured using a ^{55}Fe 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 (~ 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 ^{3}H disk source (5 cm^2) at many (~ 40) different positions in the chamber. An efficiency of ~ 10% with a uniformity of 4% has been measured. The system has a sensitivity of ~ 10^{-1} Bq/cm^2.

4. Performance of the MWPC operating at 2 atm

The use of a simple model [2] (i.e. rectilinear tracks and exponential attenuation) gives excellent predictions on the bidimensional density distributions of the center of gravity of the ionization clouds from β^- sources. For given parameters of the MWPC one finds that the shorter the linear absorption coefficient, the better is the resolving power.

We have built a second chamber, which could be operated at 2 atm; thus, the mean free path of the ^{3}H β^- rays is reduced by a factor 2 (i.e. ~ 500 μm). Furthermore we have constructed the anode plane at 45° with respect to the two cathode planes and with a wire pitch of 1 mm. In this case the spatial resolution along both directions should be dominated by the finite sampling of the avalanche process (i.e. $1/\sqrt{2}$ mm). The samples are still placed at ~ 200 μm from one cathode plane and the anode–cathode gap is 4 mm. The pitch of the cathode planes is still 2 mm with 100 μm diameter wires. Both the sample and the MWPC are contained in an aluminum box which can be pressurized up to 4 atm.

The resolving power of the system has been measured with a ^{3}H phantom of 3, 2 and 1 mm equally spaced parallel lines. As is clearly seen in fig. 2, while the 1 mm lines are not resolved at atmospheric pressure, all the three patterns are clearly visible at 2 atm.

A modulation with a 2 mm pattern which reproduces the wire pattern of the cathode nearer to the sample is also visible. This is probably due to the electric field intensification at positions along the anode wires directly underneath the cathode wires. A scan along a section orthogonal to the 3 mm and 1 mm patterns is shown in fig. 3. Once the finite extension of the source has been taken into account, a spatial resolution of ~ 800 μm (fwhm) is obtained.

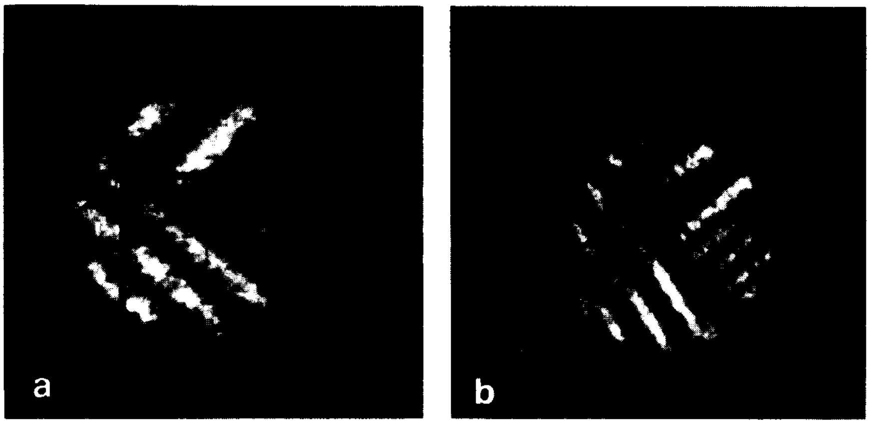

Fig. 2. The resolution ^{3}H phantom consisting of equally spaced parallel lines of 3, 2 and 1 mm: (a) analog reconstruction at 1 atm; (b) at 2 atm. (raw data).

5. Biomedical applications

The described MWPCs have been used in various biological and medical applications.

The first series of experiments was concerned with the study of variations in the ability of cell clones to incorporate a radioactive precursor of DNA biosynthesis. The biological problem has been fully described elsewhere [3,4]. In short, mammalian cell mutants with defective repair of UV-induced DNA damage can be identified by the lack of unscheduled incorporation of radioactive ^{3}H-thymidine into DNA after UV irradiation. With the MWPC all colonies with absent or low incorporation of ^{3}H-thymidine can be precisely located within a population of normally labellled 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 simulate the non-repairing cell colonies. Figs. 4b–e show 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.

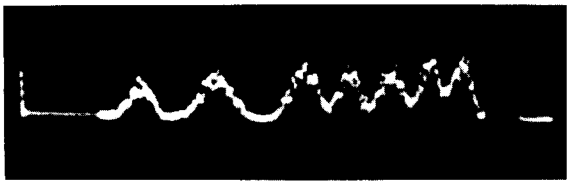

Fig. 3. Line profile of the ^{3}H phantom across the 3 and 1 mm parallel lines.

A second series of experiments was related to the use of the MWPC for the study of the regional consumption in myocardial tissue [5] with a deposit tracer of glucose

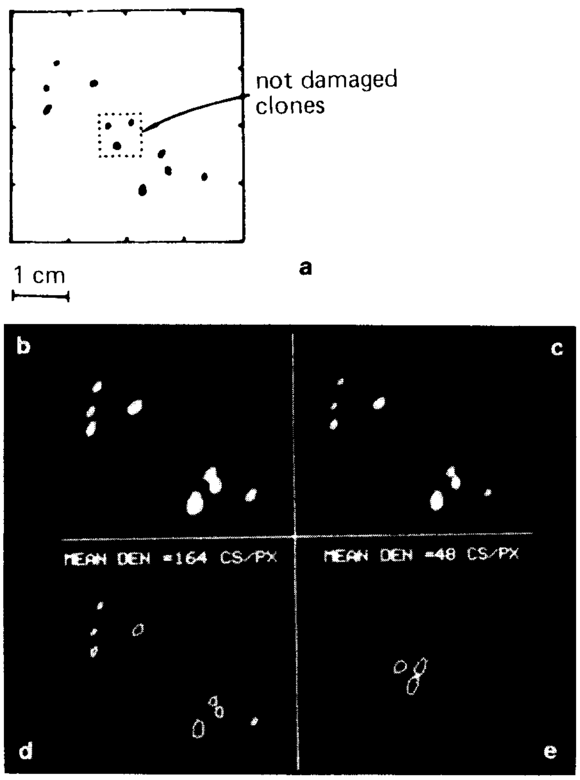

Fig. 4. Typical imaging experiment with human cells: (a) a sketch of the pattern of ^{3}H-labelled clones, (b) the original image, (c) after background subtraction, (d) the contours of the clones at 30% threshold, (e) the contour of the undamaged clones, which simulate the expected background activity in non-repairing cells.

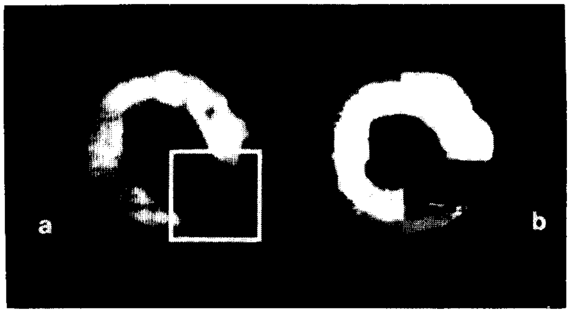

Fig. 5. Left ventricle image of the heart of a dog in which an ischemic condition was artificially induced: (a) raw data, (b) after regional computer analysis. A cold area is well evident inside the white box.

metabolism (^{3}H-deoxiglucose). Typically, 8×10^{7}Bq of ^{3}H-DG is injected intravenous to a dog. After two hours the animal is killed with an overdose of anesthetic and the heart is excised. Ultra-thin heart slices of about 40 μm 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 ^{3}H-DG distribution in a microslice 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 MWPCs 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, expecially with ^{3}H-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.

References

[1] R. Bellazzini, A. Del Guerra, M.M. Massai, M. Ragadini, G. Spandre and G. Tonelli, Nucl. Instr. and Meth. 190 (1981) 627.

[2] R. Bellazzini, G. Betti, A. Del Guerra, M.M. Massai, M. Ragadini, G. Spandre, G. Tonelli and R. Venturi, Nucl. Instr. and Meth. 204 (1983) 517.

[3] A. Abbondandolo, S. Bonatti, R. Bellazzini, G. Betti, A. Del Guerra, M.M. Massai, M. Ragadini, G. Spandre and G. Tonelli, Radiat. Environm. Biophys. 21 (1982) 109.

[4] R. Bellazzini, G. Betti, A. Del Guerra, M.M. Massai, M. Ragadini, G. Spandre and G. Tonelli, Phys. Lett. 92A (1982) 154.

[5] R. Bellazzini, A. Del Guerra, M.M. Massai, M. Ragadini, G. Spandre, G. Tonelli, P. Camici, G. Coppini and G. Valli, IEEE Trans. Nucl. Sci. NS-30 (1983) 686.

[6] G. Coppini, G. Valli, P. Camici, A. L'Abbate, R. Bellazzini, M.M. Massai and G. Spandre, submitted to IEEE Trans. Med. Imaging (1983).