can adapt itself to the existing CCTV operating conditions.

4. The system enables quicker identification of significant features in the stored image and reduces the fluoroscopy "on" time to carry out a given manipulation.

Note: All the figures have been photographed direct from the TV monitor.

Applications

This technique has potential applications in assisting difficult catheterizations, in interventional radiology and in angiography training. In all of these situations the method can be used to reduce the time of the procedure, the amount of contrast used and the radiation dose.

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Factors affecting the breathing rate of mice as used for studies of radiation damage to lungs

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Breathing rate is a useful parameter for evaluating lung function in mice after various treatment procedures which may damage the lung, including radiation doses relevant to radiotherapy. It can be measured by non-invasive, non-destructive methods, thus allowing quantitative assessment of lung changes in the same mouse over a period of time (Travis *et al.*, 1979). The method is being used regularly to assay early and late changes after irradiation of the whole lung as well as drug-induced lung injury (Travis *et al.*, 1979; 1980; Collis *et al.*, 1980).

A wide range of measured values of normal breathing rates in undisturbed mice has been reported. Rates as low as 109 breaths per minute (BPM) (Crosfill and Widdicombe, 1961) and as high as 230 BPM have been reported (Guyton, 1947; Spector, 1956). In a study of changes in breathing rate after X-irradiation of both lungs, we measured a mean rate of 330 BPM in control, unirradiated male CBA mice during quiet respiration. Because this rate was higher than the previously reported values in mice, we carried out a series of experiments in unirradiated mice to answer the following questions.

(1) Was the apparently high breathing rate observed by us in CBA mice an artefact of our testing system?

(2) How much did breathing rate depend on the strain and sex of the mice?

(3) Was there a correlation between breathing rate and relative lung weight in different strains of mice?

Apparatus and Methods

A whole-body mouse plethysmograph was used for measuring breathing rate (Travis *et al.*, 1979). Briefly, the system consisted of a clear Perspex airtight chamber with an internal volume of 125 ml. One end of the chamber was fitted with a microphone modified to act as an electrical capacitance manometer, thus converting pressure changes in the chamber into an electrical signal. The resulting signal was electronically processed and the rate of pressure changes in the chamber was recorded on a pen trace. The rate signal was calibrated over a range of known frequencies enabling the reading on the chart paper to be converted to Hz (cycles/s) which corresponded to breaths/second.

The breathing rate of ten CBA male mice, measured at fortnightly intervals over a period of one year, ranged from 310 to 355 BPM with an average breathing rate of 328 BPM (Fig. 1). Although a small but just significant decrease in breathing rate was observed with age ($p < 0.05$), even the values at one year were higher than values published in the literature.

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The breathing rate of CBA mice obtained using the plethysmograph was checked by two other methods. One technique was based on the temperature difference between inhaled and exhaled air. Thermistors were inserted in a nose cone which was placed over the snout of a CBA mouse which had been trained to accept it while being gently held in the hand. The number of temperature cycles per second was recorded on an oscilloscope. The breathing rate measured by this technique was 300 BPM, in precise agreement with the value obtained with the plethysmograph for this mouse. The breathing rate was further checked by ciné filming of a "trained" CBA mouse in the plethysmograph while simultaneously recording breathing rate on the pen recorder.* The respiratory movements of the rib cage were clearly visible when the film was projected in slow motion and counted by 12 observers. The number of thoracic movements counted varied between individual observers from 310 to 340 per minute which agreed well with the value of 336 BPM obtained from the pen recorder.

The breathing rate of unstressed, unrestrained, CBA mice was consistently within the range 300 to 345 BPM regardless of the measurement technique. It appears then that the breathing rate of this mouse strain is higher than previously reported values for mice and that the values are not an artefact of our testing system.

Biological factors

The decrease in breathing rate as a function of age (Fig. 1) is a consistent finding and could be due either to a true age related change or to acclimatization of the mice to the chamber, *i.e.* training. Aging has been reported to cause an increase in breathing rate (Mauderly, 1974). Training is a more likely influence on breathing rate in our system. Although the mice did not appear to be stressed in the chamber at any time, they were calmer in the chamber after the 20-week testing time, suggesting that training slightly influences the breathing rate. What is important is that control mice should always be tested at the same time as experimental mice.

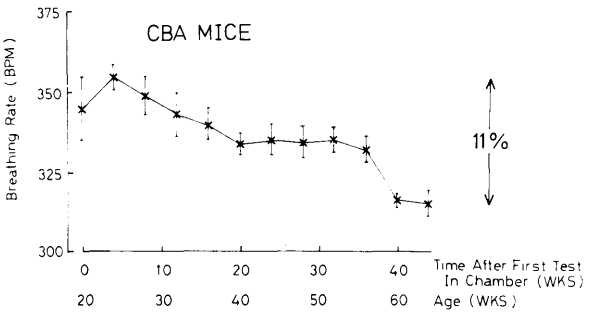

FIG. 1.

Breathing rate of male CBA mice tested at monthly intervals for one year. Each point represents the mean ±1 SEM. The breathing rate decreased with age or with acclimatization to the procedure.

The plethysmograph is large enough to permit a 25–30 g mouse to move freely in the chamber. It was found that restraining a mouse by holding gently in the hand reduced its breathing rate by about 10%. The breathing rates of three "trained" CBA mice were measured under standard testing conditions in the chamber. Each mouse was then placed in a wire mesh tube which restricted all movement. The mouse in the restrainer was placed in the plethysmograph and breathing rate recorded. Physical restraint reduced the breathing rate of the mice by 20%. What cannot be determined is whether restraint stressed the CBA mice and thus caused their breathing rate to fall in some unexpected way, or whether the restriction of movement allowed the breathing rate to be recorded during true quiet respiration. The CBA mice did, however, appear to be comfortable and relaxed in the chamber when unrestrained. Clearly the conditions of testing and handling of the mice can affect breathing rates and must be carefully controlled and uniformly maintained.

A concentration of 5% CO_2 is known to stimulate breathing rate in many species (Green, 1968). Because the plethysmograph was an airtight chamber, accumulation of expired CO_2 could cause this value to be exceeded within several minutes. The concentration of O_2 in the chamber was measured in a paramagnetic oxygen meter at timed intervals up to five minutes for seven of the "trained" CBA mice. The breathing rate was recorded simultaneously. The reduction in oxygen concentration of the respired gas after two minutes, the normal testing time, was measured as 4% (Fig. 2). Although CO_2 was not measured, it is reasonable to assume that the amount of CO_2 produced by a mouse during breathing in a closed chamber does not exceed the O_2 consumed. Therefore, in two minutes, no more than 4% CO_2 would be accumulated in the chamber, probably somewhat less, and the O_2 concentration would have fallen to 16%.

The breathing rate did not rise during this time, remaining stable up to three minutes of testing;

*Locam Camera, Ektachrome 7242, *f*5.6; film speed, 100 frames per second; viewed on 16 mm projector at silent speed, thereby reducing the speed by four.

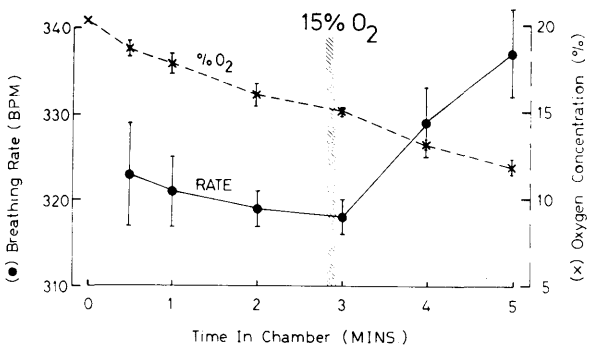

FIG. 2.

Oxygen concentration (×) and breathing rate (●) for animals kept in a closed plethysmograph for varying lengths of time. Each point represents the mean ±1 SEM for seven CBA male mice.

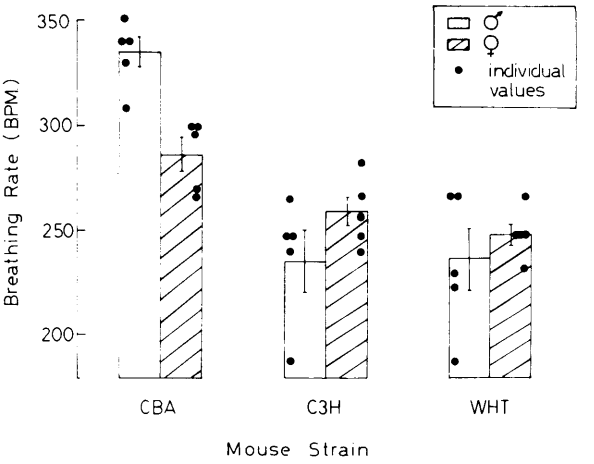

FIG. 3.

Breathing rates for male and female mice of three different inbred strains. Points represent individual animals; the error bar is 1 SEM for each group of five mice.

indeed, a slight decrease was observed (Fig.2). It appears, therefore, that the high breathing rates measured in CBA mice in the plethysmograph are not due to an increase in CO_2 in the chamber during the normal two minutes testing time. However, after three minutes of testing the breathing rate increased by 6%, as the oxygen concentration fell below 15% and the concentration of CO_2 in the chamber rose above 5%. This level of CO_2 would indeed be expected to stimulate breathing (Green, 1968). The mice also exhibited agitation and stress after three minutes, signs which are suggestive of anoxia and hypercapnia.

Previous publications on breathing rates of mice do not state the strain or sex (Crosfill and Widdicombe, 1961; Guyton, 1947; Spector, 1956). Breathing rates were measured in our plethysmograph in five mice of each sex of the three mouse strains held in the Gray Laboratory, CBA/Ht, WHT/Ht and C3H/He. All these mice were three months old and were not "trained". Breathing rate was clearly strain-dependent (Fig. 3). Both sexes of the CBA strain had a significantly higher rate than either the C3H or WHT strain ($p<0.01$ in the males and $p<0.05$ in the females). The breathing rates measured for the C3H and WHT strains were close to the upper limits of previously reported values, 235 and 237 BPM respectively. There was a clear sex dependence of breathing rate in the CBA strain only, the males having a 15% higher rate than the females ($p<0.01$). These results stress the importance of stating the strain of mice tested.

Another factor which could influence breathing rate is the size of the lungs relative to the total body (Agostoni *et al.*, 1959). The breathing rate of six untrained male CBA and five male WHT mice, six months old, was measured in the plethysmograph and the mice were then weighed and killed by ether anaesthesia. The lungs were rapidly removed from the thorax, cut from the bronchus, blotted and weighed. The ratios of wet lung weight to body weight in the two strains indicated that the CBA mice have lungs about 18% smaller than those of WHT mice (Table I). The breathing rate of the CBA mice was 38% higher than in the WHT males. The higher breathing rate in the CBA mice may be necessary to compensate partially for the relatively small lung size in these mice.

TABLE I

RATIO OF LUNG WEIGHT TO TOTAL BODY WEIGHT IN TWO MOUSE STRAINS

Group	Body weight (g)	Lung weight (g)	Lung wt. / Body wt.	Breathing rate (BPM)
CBA/Ht (5)				
Mean	32.453	0.135	0.004	330
SEM	1.226	0.002	0.0001	
WHT/Ht (5)				
Mean	35.313	0.175	0.005	248
SEM	0.996	0.007	0.0002	

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Technical notes

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Induced radioactivity in patients from betatron irradiation

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The nuclear binding energy averages 7–8 MeV per nucleon. If a nucleus is penetrated by a quantum of energy which exceeds this average binding energy, the nucleus may lose one or more of its nucleons. The residual nucleus may be radioactive. As early as 1949, induced radioactivity in tissue from a 24 MeV synchrotron was demonstrated by Mayneord *et al.* (1949). This induced radioactivity results from the nuclear photo-effect and accounts for less than 1% of the total energy absorbed from a bremsstrahlung spectrum whose average energy is 10 to 15 MeV (Joyet, 1965). Since this correlates with energy levels used clinically in betatron irradiation, the induced activity may be useful in clinical applications, including correlation of the activity distribution and ultimately the dose distribution with that prescribed by the clinician. A similar visualization procedure for a therapeutic proton beam has been demonstrated using an on-line positron camera (Bennett *et al.*, 1978).

MATERIALS AND METHODS

The 33 MeV Brown Boveri betatron at Montefiore Hospital and Medical Center was utilized for this research in a clinical setting. Patients already undergoing radiation with standard treatment fields and fractionation schedules of 200–300 cGy (rad) were randomly selected for measurements of induced radioactivity.

Immediately after treatment the patient was brought to an enclosed area adjacent to the betatron room. A sodium iodide crystal was positioned on each side of a movable bed on which the patient rested (Fig. 1). By moving the bed it was possible to vary the position of the treatment field relative to the sensitive volume of the detector pair. The detectors were separated by 65–70 cm and were connected to discriminators with threshold just below the photopeak for annihilation radiation. Fast coincidences were fed to a multichannel analyser in multi-scaling

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