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GENERATOR-PRODUCED KRYPTON-81m FOR DYNAMIC STUDIES OF THE LUNGS AND HEART WITH THE SCINTILLATION CAMERA

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DISCLAIMER

Generator-Produced Krypton-81m for Dynamic Studies of the Lungs and Heart With the Scintillation Camera

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ABSTRACT

Krypton-81m is obtained in multimillicurie amounts from its cyclotron-produced parent isotope 4.7-hr rubidium-81. The 13-sec ^{81m}Kr daughter decays by isomeric transition and emission of a monoenergetic 190-keV γ-ray which is 35% internally converted. Dynamic perfusion studies are done with ^{81m}Kr by injecting the sterile saline-^{81m}Kr solution intravenously and taking 1- to 3-sec exposures with the scintillation camera. Blood flow through the right heart, pulmonary arteries, and lungs is visualized. Krypton-81m is obtained as a gas from the same generator system by eluting the dry resin column with air. This mixture of ^{81m}Kr and air is inhaled by the patient to provide ventilation and exchange studies of the lungs. Five to six mCi of ^{81m}Kr can be given every few minutes to obtain different views or to repeat studies of patients. The high photon yield, moderate γ-ray energy for scintigraphy, and short half-life (which keeps the radiation dose to a low level) make ^{81m}Kr an ideal radionuclide for dynamic studies with the scintillation camera.

INTRODUCTION

Studies of pulmonary function with radioisotopes usually involve the evaluation of regional pulmonary perfusion with labeled aggregates or the assessment of pulmonary ventilation and exchange capacity with radioactive gases. Most perfusion studies are now being done with aggregated particles of albumin or hydrous ferric oxide labeled with radioisotopes such as iodine-131 [1], technetium-99m [2], or indium-113m [3]. Ventilation and exchange studies as well as perfusion studies are being done with the radioactive inert gases xenon-133 [4] and krypton-85. Wagner has reviewed the use of radioactive noble gases for assessment of ventilation and perfusion in lungs and the regional flow of blood in other areas [5]. Other studies are being done with the very-short-half-life gases such as ^{15}O, ^{11}CO, and $^{11}CO_2$ [6]. These short-half-life isotopes must be used near the cyclotron where they are produced.

We have been using the radioactive inert gas krypton-81m, which is obtained from a ^{81}Rb-^{81m}Kr generator [7]. This is a further development of generator-produced short-lived radionuclides for visualizing blood

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vessels and organs [8]. ^{81m}Kr is useful for dynamic blood flow studies through the major blood vessels, right heart, and lungs, using short exposure times of 3 to 5 sec with the scintillation camera. The short half life and rapid excretion of ^{81m}Kr allow giving 5 to 6 mCi while keeping the radiation dose to the patient at a low level. Jones and Clark have also described a ^{81m}Kr generator for cardiopulmonary studies with the scintillation camera [9].

Krypton-81m, which decays with a half-life of 13 sec, can be milked every few minutes from its 4.7-h parent isotope ^{81}Rb. The 190-keV γ-ray energy of krypton-81m is more favorable for scintigraphy than the 81-keV γ-ray emission of xenon-133 which is attenuated by bone and tissue.

Figure 1 shows the decay scheme for both the 4.7-h ^{81}Rb parent and the 13-sec ^{81m}Kr, which decays by isomeric transition and emission of a 190-keV γ-ray (65% abundant and 35% internally converted) to ^{81}Kr. The ^{81}Kr decays by electron capture with a half-life of 2.1 x 10^5 y to stable ^{81}Br [10].

METHODS AND MATERIALS

The parent isotope ^{81}Rb is produced by irradiating about 400 mg of reagent-grade NaBr with 50-MeV α particles in the Lawrence Radiation Laboratory 88-inch cyclotron. The nuclear reaction on the nonenriched, 49.5%-abundant ^{81}Br is $^{81}_{35}Br(^4_2He, 4n)^{81}_{37}Rb$, which has a threshold energy of 30.8 MeV. The yield of ^{81}Rb averaged from four production runs is 2.9 MCi/μA-h, if an average beam current of 15/μA is used.

Rubidium-81 could also be produced by ^3_2He particles from a small cyclotron, either by the nuclear reaction $^{81}_{35}Br(^3_2He, 3n)^{81}_{31}Rb$, Q-value -12.2 MeV, or $^{79}_{35}Br(^3_2He,n)^{81}_{37}Rb$, Q-value 6.6 MeV.

The radiation level from the NaBr target, after irradiation with 50-MeV α particles for 25 μA-h, is >50 r/h at 6 in. Because of this high radiation field it is necessary to use at least 2 inches of Pb shielding during the processing of the target material. All the processing of ^{81}Rb is done in a Pb "cave" by remote operation from outside the shielded area.

The NaBr target material is washed from the powder plate holder with a stream of sterile distilled water into a sterile 250-ml flask and diluted to a volume of 125 ml. This dilution is necessary to reduce the concentration of NaBr, because salt solution >0.5% displaces the ^{81}Rb parent from the ion-exchange column.

The parent ^{81}Rb is retained on strongly acidic cation-exchange resin composed of nuclear sulfonic acid exchange groups attached to a styrene-divinylbenzene polymer lattice (Bio Rad AG 50 x 4, 200-400 mesh). This resin in the hydrogen form is held in a specially constructed Pyrex column 11 mm i.d. and 60 mm high and fitted with Luer-lock connections at the top and bottom. The electrical-motor-driven elution apparatus shown in Fig. 2 has been described previously [11]. The eluate solution of sterile H_2O is mixed with an equal volume of 2% NaCl solution below the resin column to give an isotonic saline solution for administering ^{81m}Kr by intravenous infusion for lung perfusion studies.

Sterile and pyrogen-free reagents and equipment are used for the procedure. The solution flows through an in-line Millipore filter (0.45 μ) just before intravenous infusion. Sample elutions from each production generator have been checked by an independent laboratory and found to be sterile and pyrogen free.

The generator is shielded with 3.75 in. of Pb consisting of 1.75 in. of interior shielding plus 2 in. of outer shielding which is built up from 0.25-in. thick half-circle layers. This shielding is necessary because of the high radiation level at the surface of the resin column. The radiation from the shielded generator does not interfere with the operation of the scintillation camera even when the generator is located within 2 feet of the camera head.

With 50 mCi of ^{81}Rb on the resin column, elution with 5 ml of H_2O will yield about 5 mCi of ^{81m}Kr. The leakage of ^{81}Rb for each elution is 10^{-5} part of the total ^{81}Rb on the column. The usual injected dose for perfusion studies is 5 mCi of ^{81}Kr with less than 0.5 μCi of contaminating ^{81}Rb.

The radiation dose to a 70-kg human subject for each study is calculated to be 3.8 mrad to the lungs from 5 mCi of ^{81m}Kr and 3.9 mrad to the heart and kidneys from 0.5 μCi of ^{81}Rb. These calculations were made assuming the biological half time to be equal to the physical half-life of the isotope.

Gaseous krypton-81m can also be eluted by rapidly forcing 50 ml of air through the dry resin column. The ^{81m}Kr is inhaled directly by the subject through polyethylene tubing. The yield of ^{81m}Kr for each elution is about 5 to 6 mCi from a 50-mCi generator. It is possible to do either H_2O elution for perfusion studies, or air elution for ventilation studies, using the same ion-exchange column by attaching a sterile three-way valve control and a sterile 50-ml syringe to the "saftiset" tubing that connects the eluant H_2O reservoir to the automatic two-way valve leading into the ion-exchange column (Fig. 2). With the syringe plunger of the central column syringe in the lowered position to reduce the air space above the column, filtered air is taken into the 50-ml syringe and forced through the resin column until all the liquid is pushed through the column and its connecting polyethylene tubing. This usually requires about 100 ml of air. Thereafter 50 ml of air can be forced through the resin column to provide ^{81m}Kr in gaseous form. By reconnecting the H_2O reservoir in place of the 50-ml air syringe, perfusion studies can again be done without altering the low leakage characteristics of the ion-exchange resin for ^{81}Rb.

RESULTS AND DISCUSSION

To determine the anatomical, physiological, and diagnostic information that can be obtained by using ^{81m}Kr, preliminary studies have been done on five normal volunteers and eleven patients with known respiratory problems. The subjects have been asked to breathe at specified intervals and to control the rate and depth of respiration in certain instances. There has been no spirometric control for the studies reported here.

For perfusion studies, ^{81m}Kr in 10 ml of isotonic saline was infused for 3 to 5 sec into the right antecubital vein. The patient was lying either supine or prone. Serial scintiphotos were taken, using exposure times of 2 to 5 sec while the patient held his breath. The depth of inspiration varied from normal to maximum. The tracer usually leaves the right heart within 15 sec after the infusion is started. In dynamic cardiac studies a 10- to 20-sec exposure was taken at the end of the study to show the distribution within the lungs. Further pictures were then taken as the patients breathed at their usual rate and depth, exposures being terminated when sufficient dots were recorded. Within 2 min, activity falls to a level that no longer permits pictures to be taken.

For ventilation studies, 50 ml of air was forced through the dry generator with a 50-ml syringe. In some instances the patients were asked to inhale through a short length of tubing 1 cm in diameter over a period of 5 to 15 sec, from forced expiration to maximum inspiration, as the 50 ml of air carrying the ^{81m}Kr was directed into the tubing. A nose clip was used and the studies were performed with the patients in supine and prone positions. Because of the short half-life, it is not possible to achieve an equilibrated state when breathing ^{81m}Kr, and only single-breath respiratory studies have been performed. The exhaled radioactivity was removed via an exhaust system. The exhaled gas should not be allowed to collect immediately adjacent to the camera. If it is not swept away it drifts along the table upon which the patient is lying and produces odd patterns on the scintiphotos.

The positions of the lungs and heart in the camera field were determined by a transmission picture taken with a collimated disk source of ^{99m}Tc placed below the patient, as suggested by Anger and McRae [12]. The area of normal lung transmission was compared with the distribution of radioactivity in both the perfusion and ventilation studies.

Figure 3 shows ventilation studies on two normal subjects. Inhalation of gaseous ^{81m}Kr began from maximum expiration. In the case of J.M., a 40-year-old male, ^{81m}Kr was administered during normal inspiration, whereas in D.V.D., a 46-year-old male, ^{81m}Kr was given continuously during steady inspiration lasting 10 sec. The trachea and major bronchi can be recognized, and in the slower inspiration the outward spread of radioactivity is apparent.

Figure 4 (A.H. 3-11-69), left, shows a normal distribution of ^{81m}Kr infused in saline solution as seen in an anterior view. At the top is the transmission picture, which defines the field of view and shows the position of aerated lung. Below and to the left are 4-sec exposures of the dynamic study and at the bottom is a picture taken from 30 to 60 sec postinfusion. In the 8- to 12-sec scintiphoto the left ventricle is outlined as an area of diminished radioactivity lying between the right ventricle and the left lung. At the right is the ventilation study of the same patient. The ^{81m}Kr was administered as rapidly as possible as the patient took a deep breath. The tracheo-bronchial tree was not demonstrated. The distribution of activity is similar for both perfusion and ventilation studies, and it corresponds to the transmission picture of the lungs.

SUMMARY

Krypton-81m has favorable characteristics for imaging with the scintillation camera. It has an ideal γ-ray energy with high photon yield, low radiation exposure, and a short physical half-life that allows rapid repeat studies. The 4.7-h half-life of the parent makes studies possible throughout one day. A method has been presented for obtaining millicurie amounts of ^{81m}Kr in solution or as a gas from the ^{81}Rb parent.

Preliminary perfusion and ventilation studies have been done on five normal volunteers and eleven patients to determine the type of physiological and clinical information which can be obtained by using the dynamic and static imaging capabilities of the scintillation camera. Excellent resolution of the right heart, left and right pulmonary arteries, and upper tracheobronchial tree has been achieved. Also it has been possible to watch the changing distribution of activity as inhalation proceeds. Abnormalities have been demonstrated in patients. Krypton-81m should be particularly useful to determine the variations in distribution of activity within the lungs in various lung disorders with changing patterns of inhalation. The inability to follow washout patterns and to achieve an equilibrated condition by breathing a fixed concentration of radioactive gas, as has been done with ^{133}Xe, limits the type of study which can be performed, but how important this limitation will be remains to be investigated. Unlike ^{133}Xe, which must be washed out of the lungs for periods of up to 15 min in abnormal cases, ^{81m}Kr rapidly decays within 2 to 3 min, so that multiple studies can be completed in a short time.

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FIGURE CAPTIONS

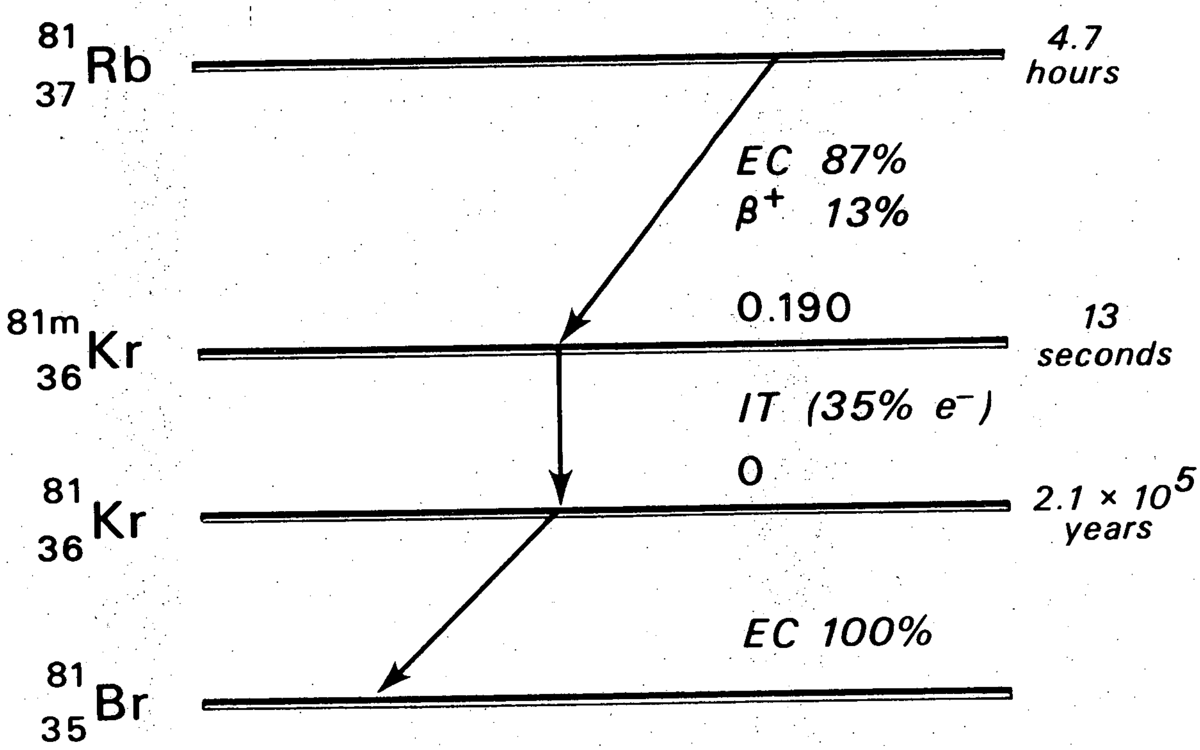
Fig. 1. Decay scheme for ^{81}Rb - ^{81}Kr.

Fig. 2. Radioisotope generator system for ^{81}Kr (external shielding open) visible are automatic two-way valve, resin column, polyethylene tubing, sterile H_2O for elution, and 2% NaCl solution.

Fig. 3. Ventilation studies of two normal subjects.

Fig. 4. Normal distribution of ^{81m}Kr in perfusion (L) and ventilation (R) studies.

RUBIDIUM-81, KRYPTON-81m DECAY



DBL 704-5679

Fig. 1

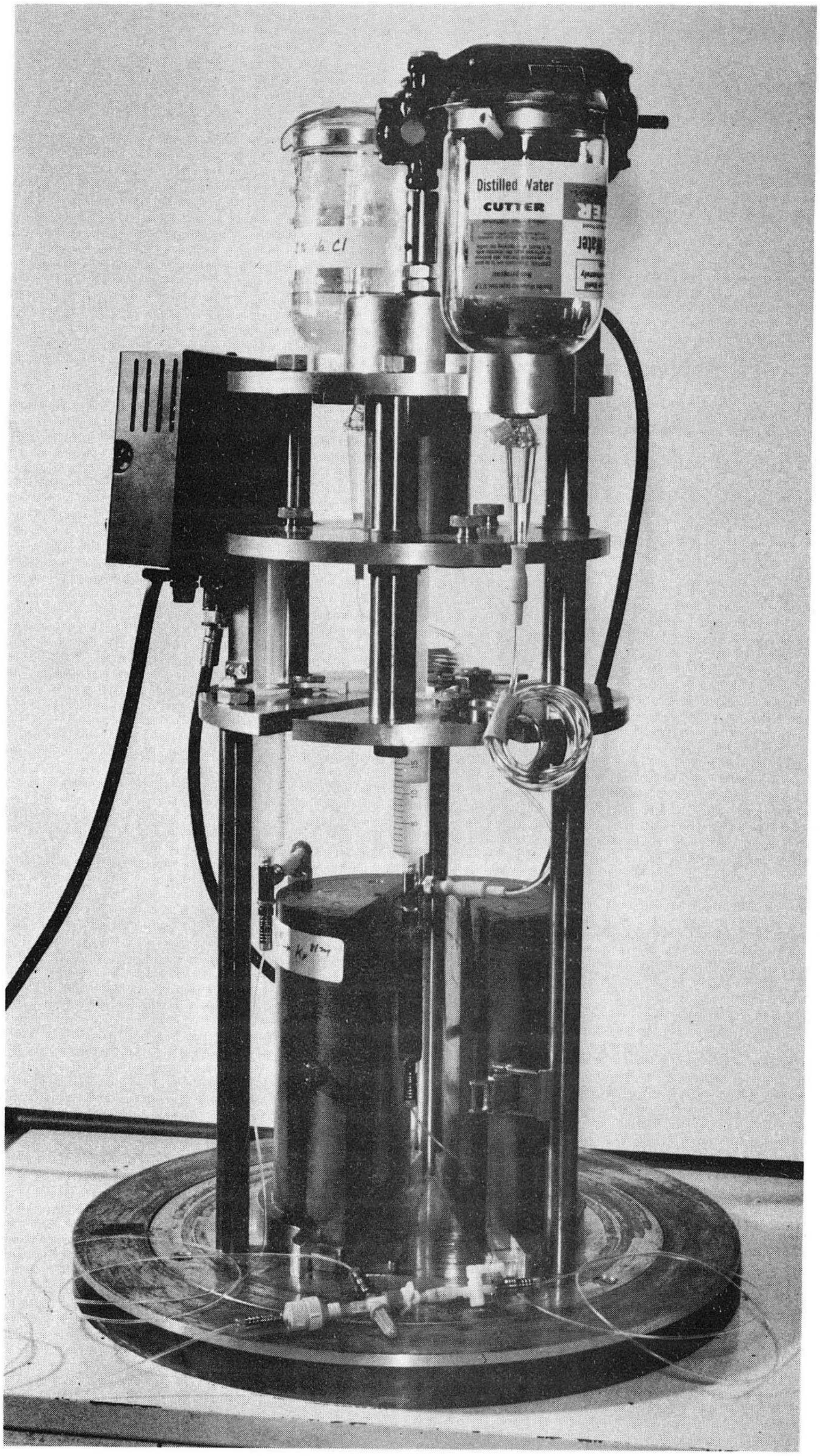


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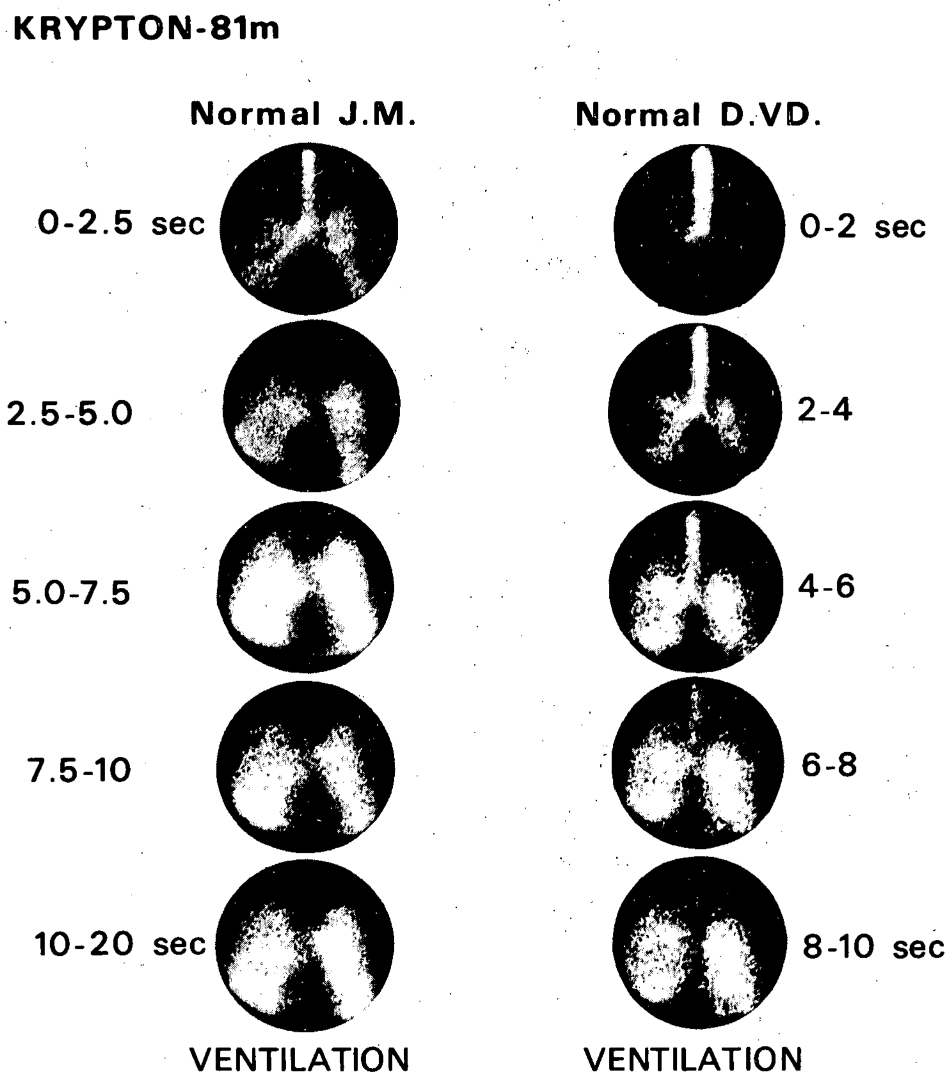
Fig. 2



XBB 696-3853

Fig. 3

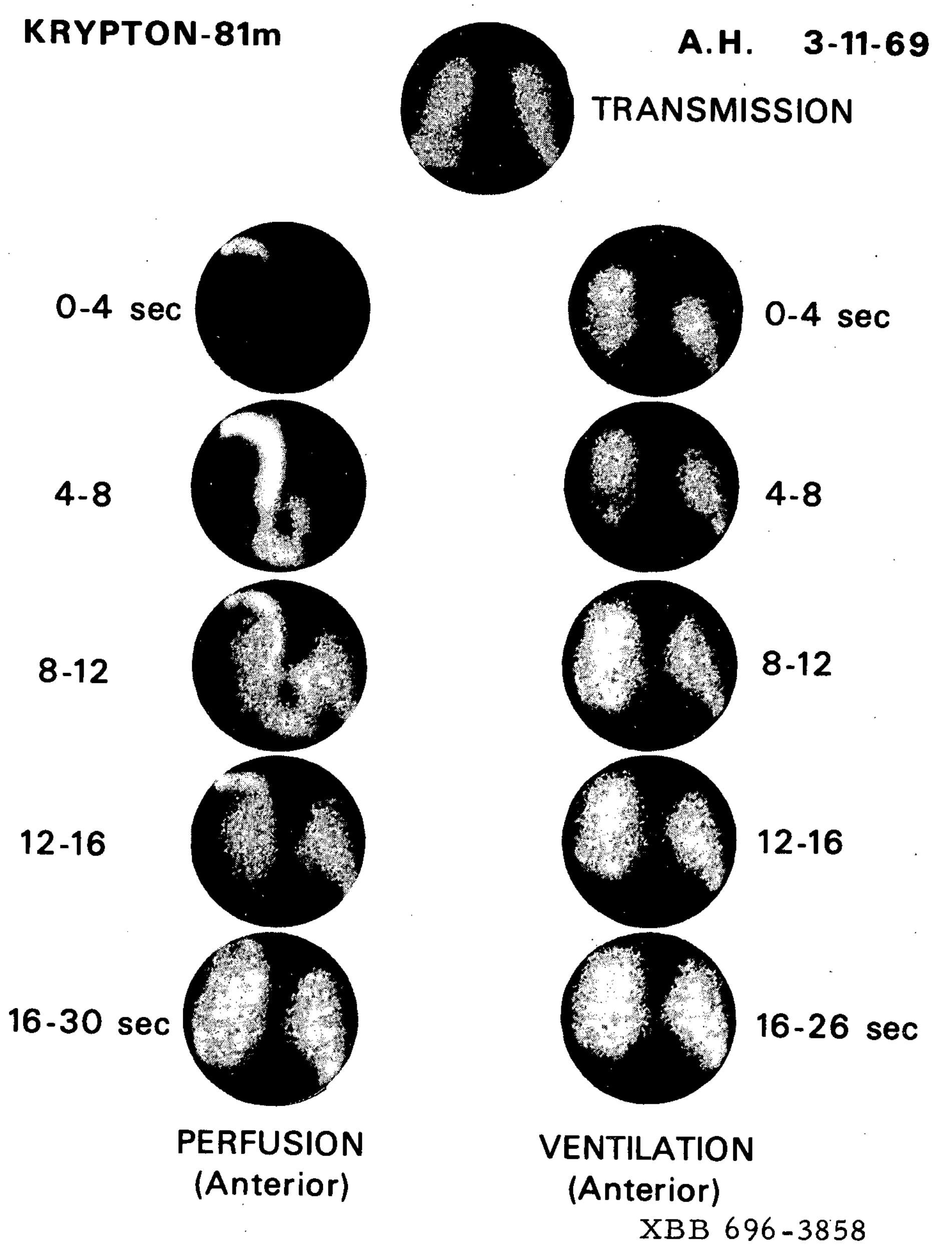

KRYPTON-81m
A.H. 3-11-69
TRANSMISSION
0-4 sec
4-8
8-12
12-16
16-30 sec
0-4 sec
4-8
8-12
12-16
16-26 sec
PERFUSION
(Anterior)
VENTILATION
(Anterior)
XBB 696-3858

Fig. 4

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