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Measurement of nasal mucociliary transport rate in normal man

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SUMMARY

After reviewing the main methods excisting to calculate the rate of the mucociliary transport, the authors describe their personal technique. A ^{99m}Technetium Sulphur Colloid drop is deposited in the nasal fossa, which is carried away by the cilia down to the rhinopharynx and followed by a gamma camera. To calculate the transport rate, a new method of quantification has been introduced, based on the formation of a parametric image. A study was carried out in 14 males without any pathology of the upper airways, obtaining a mean velocity of 5.3 mm per min (range 3.3.-8.2).

INTRODUCTION

The first attempts to show the nasal mucociliary function are those made by Martius in 1884 by means of stroboscopy, and he managed to calculate the beat frequency of the cilia. His method was later developed by other authors but, as it happens with photographic and cinematographic techniques, it does not possess the most suitable conditions for clinical experimentation. All these methods are expensive and have a remarkable technical complexity.

More effective methods, specially in order to calculate the speed of mucociliary transport, are those based on the pursuit of particles introduced in the nasal cavity down to their fall into the pharynx. The first studies were made introducing coloured particles into the nasal fossa and calculating the time they took to appear in the pharynx (Hilding, 1931; Tremble, 1948). More sophisticated methods are the "radioactive" ones. They consist in the introduction of a particle labeled with a radioisotope into the nasal cavity and seeing how it moves upon the cilia. Apart from some "pioneer" studies that used I^{131} (Proctor and Wagner, 1965), the radioisotope preferred is the ^{99m}Technetium. This product, introduced in literature by Harper et al. in 1962, has proved to be the most effective for the main part of explorations that need radioisotopes, and very specially for the calculation of the mucociliary transport rate.

MATERIALS AND METHODS

Twenty persons have been examined, six of whom had to be excluded from the

study because of movements of head during detection, and also due to dubious deposition of the radioactive drop on the nasal mucosa. The fourteen persons whose detection was good enough to be enclosed in the study were males with a mean age of 46 years (range 23 to 62) without any kind of pathology of the upper airways.

Our method, which follows the one described by Quinlan et al. (1969) and Proctor and Andersen (1976), consisted in placing a drop of Tc-99 Sulphur Colloid on the superior surface of the anterior end of the lower turbinate of one nostril, the patient in supine position and with his head lateral under the gamma camera. In this way we intended to avoid any influence of gravity on the drop motion over the mucosa. The drop contained 25 microliters measured with a micropipette, and the radioactivity was approximately 37 Megabequerels (MBq).

Each study lasted thirty minutes, taking analog images every ten minutes. At the same time the studies were recorded in a computer, one image per minute in a 64×64 word matrix type. We used a Picker Dyna 4/15 Gamma camera fitted with a low energy, high resolution collimator, and connected to a digital PDP 11/34 computer (Figure 1). The processing of the studies included first a time and space smoothing. Further, a time-of-arrival parametric image was obtained by means of a FORTRAN IV program. Each pixel of this image contains the time taken by the

Figure 1. (From left to right and from above to below) Pathway of the drop marked with Tc-99 from its placing in the anterior end of the turbinate down to its arrival to the rhinopharynx. At the beginning it has a low intensity, which increases as it moves forward in the direction marked by the tracer.

tracer to arrive at a certain point if such a point is located within the pathway of the sulphur colloid drop.

The method used for calculation is schematically described in Figure 2. For every elemental time-activity curve the time of arrival is calculated as the time taken to surpass a threshold (mean $\pm$ 2 SD) previously calculated in a background area of the pathway. If through the study no activity reaches a determinate pixel, the contents of that pixel will be zero. This gives us the complete track left by the tracer while passing through the nostril, the beginning of the track having a low inten-

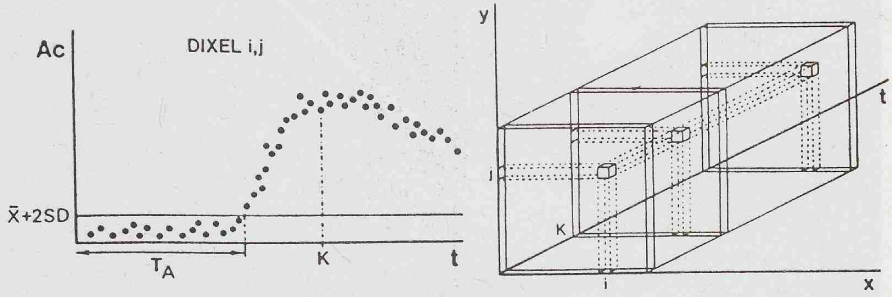

Figure 2. Elemental time-space curve corresponding to the pixel in position i, j, through the 30 minutes. For each one of these curves the time of arrival is calculated, and the value placed on the pixel in the same position (i, j). In this way, the parametric image is generated.

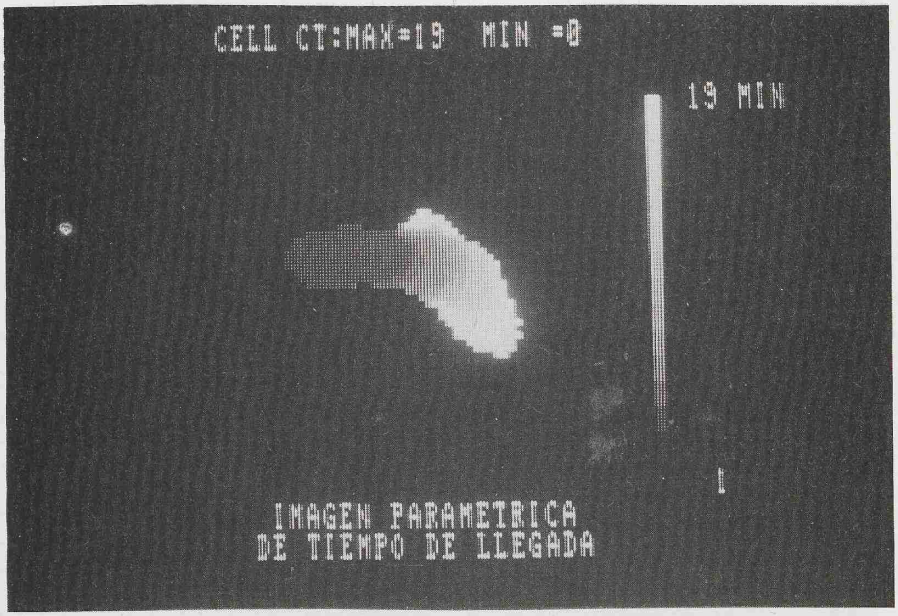

Figure 3. Time-of-arrival parametric image. Each pixel contains the time taken by the tracer in arriving to that position from the beginning of the study. An increase of activity is observed in the direction of the movement.

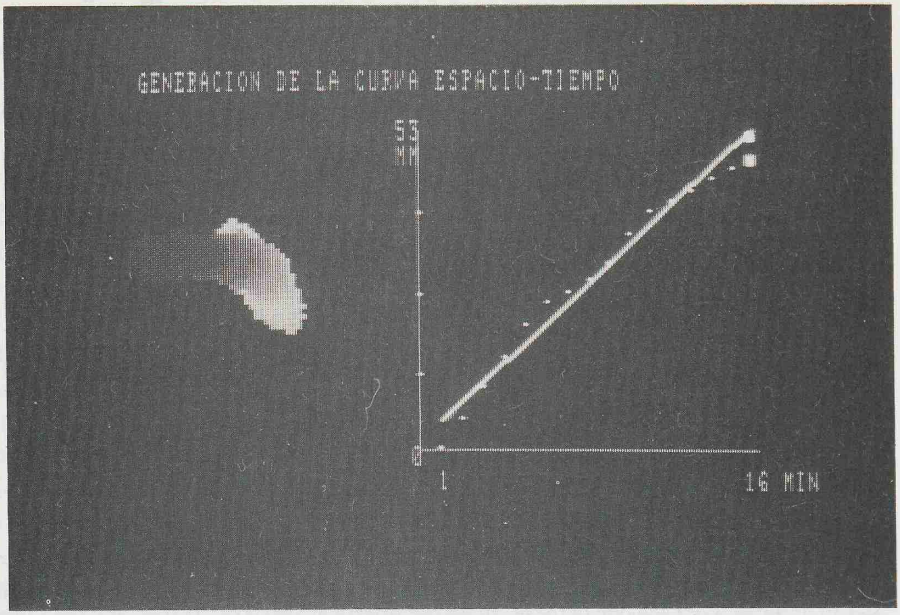

Figure 4. Curve space versus time corresponding to the movement of the drop. Dotted line, raw data; continuous line, least square fit to obtain the mean velocity in the fragments of the trajectory previously chosen.

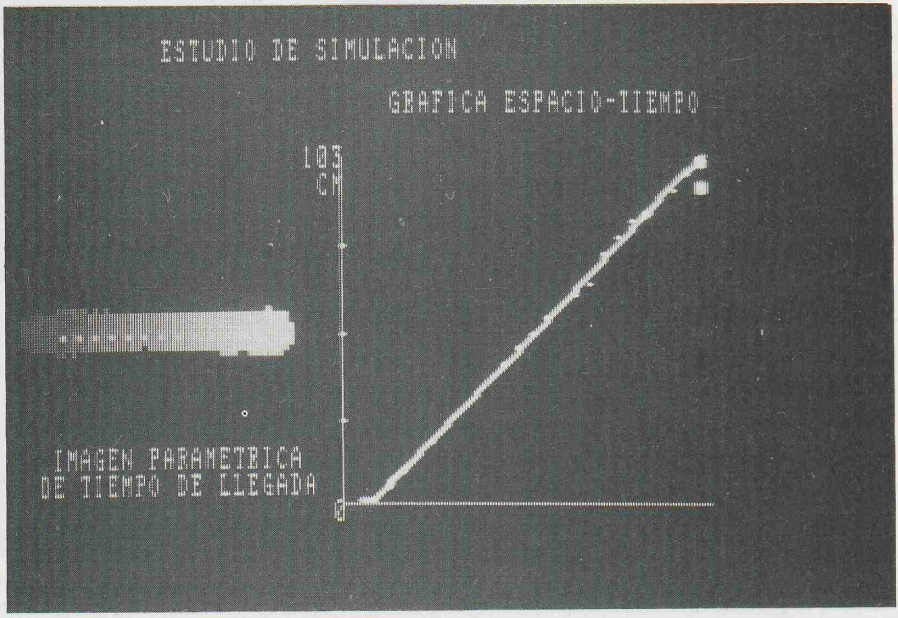

Figure 5. Parametric image and curve in the simulation test.

sity which rises whilst advances in the direction followed by the tracer (Figure 3). Then up to 12 consecutive ROIs (Regions Of Interest) of 1 pixel each are marked on the track starting from the pixel where the drop has been placed and following its direction. The distance between each pixel and the former is the space covered by the drop, and the difference between their contents is the time spent in covering it. These data are used to generate the time-space curve corresponding to the motion of the tracer (Figure 4). From the time-space curve we can calculate the transport rate in any fragment of the pathway by only fitting a linear least-square regression to the points forming that fragment. To give the space in length units we previously calculated the size of one pixel placing two spot radioactive sources on the collimator surface separated 10 cm one from the other. We obtained a 2.56 mm/pixel factor.

Our method of analysis was validated by giving a slow and even movement to a small radioactive source and recording its motion with the computer. The velocity obtained using our method coincided with the velocity given to the source (Figure 5).

The subjects were studied in the same room, where the temperature (22 ± 2 °C) and relative humidity (45 ± 5%) were controlled and remained constant.

RESULTS

The results of our study are presented in Table 1. We obtain a mean rate of transport of 5.3 ± 1.4 mm per minute; the range is 3.3 to 8.2.

We do not find any difference between young men and older people: a man aged 62, for example (case no. 9) has a faster rate than the cases nos. 8 and 10, 23 and 26 years-old respectively; but the 13, 61 years-old, has a very slow velocity.

Table 1.

case no.	age	rate (in mm/min)	
1	40	4.9	
2	44	4.7	
3	47	5.8	
4	58	6.7	
5	52	6.1	
6	50	5.7	
7	41	6.3	
8	23	3.8	
9	62	8.2	
10	26	4.1	
11	56	6.4	
12	54	3.9	n = 14
13	61	3.3	mean = 5.3
14	30	4.4	SD = 1.4

DISCUSSION

The speed of the nasal mucociliary transport is a highly variable parameter, even in identical environmental conditions. The data obtained from the main articles on this subject appear in Table 2. We present only the mean rates, because all these authors recognize its extreme variability: Proctor and Andersen (1976), for example, obtain a mean rate curiously identical to ours, but they talk of a very wide range: 0.5 to 23.6 mm per min, whereas we present a more limited margin: the maximum speed is 8.2, the minimum 3.3. We consider extremely important to delimit exactly the velocity of mucociliary transport because it shows us a useful information about the functionalism of every stage of the respiratory tract. We can see alterations of it in laryngectomees, in the Kartagener syndrome, and in any pathology of the lower airways.

Table 2.

Ewert (1965)*	4.2 mm/min
Quinlan et al. (1969)	7 mm/min
Andersen et al. (1971)	5 mm/min
Guillerm et al. (1971)	6 mm/min
Proctor and Andersen (1976)	5.3 mm/min
Simon et al. (1977)**	6.6 mm/min
Sackner (1978)*	7.5 mm/min
Robert et al. (1980)	8.3 mm/min
Karja et al. (1982)	9 mm/min

* with non-radioactive methods.
** with ^{51}Cr.

We believe that the technique we have followed in this study is easy and produces little discomfort to the patient. The main drawbacks met are, on the one hand, the accuracy in placing the drop on the mucosa: the end of the micropipette would not be drawn over the epithelium, and the sulphur colloid must be dropped off with care, otherwise the drop splashes and the image is displayed as a big initial spot of activity which superposes on the following frames making impossible to mark one-pixel ROIs. On the other hand, the patient must remain motionless, otherwise slight movements of his head lead to erroneous calculation of the velocity. For this reason, six of our subjects have been rejected. Perhaps this could have been avoided placing a source of ^{57}Co on the subject's face out of the drop trajectory. This would permit not only the detection of movements but also their correction.

In spite of the drawbacks mentioned we believe this technique very useful in the assessment of the transport function of the nasal mucociliary system. The introduction of a parametric image makes the calculation easier, being furthermore a reliable method as demonstrated by the simulation test.

RÉSUMÉ

Après avoir passé en revue les principales méthodes existantes pour calculer la vitesse du drainage mucociliaire nasal, les auteurs décrivent leur technique personelle. Celle-ci consiste en déposer une goutte de ^{99m}Technetium dans la fosse nasal et suivre son traject jusqu'a la rhinopharynx avec une gamma caméra. On présente une nouvelle méthode pour calculer la vitesse du transport mucociliaire, basée dans la formation d'une image paramétrique. L'étude fut réalisé avec 14 sujets mâles, avec des âges compris entre les 23 et les 62 ans et sans aucune pathologie respiratoire; on obtient une vitesse moyenne de 5.3 mm/min (maximum 8.2, minimum 3.3).

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