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| Author(s)    | 金田, 弘; 前田, 盛正; 新田, 輝夫 他   |
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## FURTHER CONSIDERATIONS ON THE SIEVE.

Hiromu KANEDA, Morimasa MAEDA, Teruo NITTA  
and Kazuo YAMAMURA

Department of Radiology, Kyoto Prefectural University of Medicine.

(Director: Professor Dr. Hiromu Kaneda)

## 篩照射法に使用する篩の検討

京都府立医科大学放射線医学教室 (主任 金田 弘教授)

金 田 弘 前 田 盛 正  
新 田 輝 夫 山 村 和 夫

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レ線篩照射法に用いている篩は面積比4:6, または5:5, 開放部の大きさ5—10mm直径のものが標準とされているが, これは主として臨床経験的に得られたものであつて, 基礎的な研究の結果得られたものではない. この論文は一般に標準と考えられている篩が篩照射法の実際において, はたして適当であるかを種々なる角度より検討したものである. まず篩の配列について考察し, 鉛板に多数の穴を開けた篩は, これと逆の篩よりも生物学的篩結果が高いことを全身照射したマウスの生存率より実証するとともに, Jalles の用いている弁慶縞様の篩もまた篩効果の面よりすぐれていることを知り得た. 次に開放部の大きさについては, その1つ1つが小さいほど生物に及ぼす障害は軽度であるが, これにも限界があり, 面積比4:6または5:5の篩では, 5mm直径が最小の限度ではないかと考えている. 第3に面積比について検討し, 種々なる面積比の篩を用いて同一

容積線量を照射した実験により6:4の篩では均等照射よりもマウスの生存率が低下することを知り, 均等照射よりも生存率が高い5:5, または4:6面積比が生物学的篩効果を得る上にも適当ではないかと考えている. 2:8の篩では照射線量が大量であり, 開放部に一致して脱毛を認めたにも拘らず生存率が照射しない対照群と殆んど変わらないことは注目に価する. 第4として篩照射法の実際において分割照射毎に篩を一致せしめた方がよいかを家兎耳介の穿孔線量にて検討し, 一致せしめた方が穿孔せしめるに要する線量が多く, 生物学的篩効果率は3.8であるが, 一致せしめず万偏なく照射した場合には1.4であることを知り得た.

以上のごとき結果より, いわゆる標準型の篩は高い生物学的効果を得る上にも適当であることを認めた.

From the time that sieve therapy was first tried by Köhler<sup>1)</sup> in 1909, various types of sieve have been used by many workers. Köhler used a sieve made of wires 1 mm thick with spaces 2 mm wide to irradiate with ten or fifteen times the maximum tolerable skin dose at that time.

Liverson<sup>2)</sup> (1933) employed a sieve with openings varying from 8 mm to 20 mm in diameter which permitted 50 per cent of a direct beam to pass. Grynkrant<sup>3)</sup> (1935) design-

ed a sieve with a square lattice arrangement with openings of 9 cm<sup>2</sup> between solid strips 1 cm wide.

Haring<sup>4)</sup> (1934) noted that the therapeutic results with interstitial application of radium needles in the therapy of cancer were superior to those of conventional radiation treatment and employed a sieve with openings 3 mm in diameter to enable the use of a dose equivalent to that given with radium needling.

No further advances in sieve therapy occurred until 1949, when Jolles<sup>5)</sup> reported fundamental studies on this problem.

Jolles advocated a lead sieve with chessboard arrangement alternating opaque and transparent 1 cm squares.

The sieve used by Marks<sup>6)</sup> (1950) was lead rubber with square apertures ranging from 0.25 to 4 cm<sup>2</sup> and allowing 40 per cent transmission through the portal. With 1 cm apertures he delivered to the suprapubic region a daily dose of 1,500r for 18 treatments over a period of 24 days with X-ray of 0.9 mm Cu. h.v.l. (total dose 24,000r).

As indicated in table 1, a sieve with circular apertures 1 cm in diameter allowing 40 per cent transmission through a portal has been in general use and this type of sieve is considered as the standard one.

But the fact that this type of sieve is most suitable, was not obtained from funda-

Table 1.

| Authors                    | Year | Size of Opening | Area ratio         |
|----------------------------|------|-----------------|--------------------|
| Liberson                   | 1933 | 0.5 sq. cm.     | 50 : 50            |
| Grynkrant                  | 1935 | 3               | 64 : 36            |
| Loevinger<br>Minowitz      | 1950 | 1.8<br>1        | 40 : 60<br>40 : 60 |
| Marks                      | 1952 | 0.5<br>1<br>1.5 | 40 : 60            |
| Tenzel                     | 1952 | 1               | 40 : 60            |
| Harris                     | 1952 | 0.5<br>1<br>1.5 | 40 : 60            |
| Loevinger                  | 1952 | 1               | 40 : 60            |
| Cohen, Palazzo             | 1952 | 1               | 50 : 50            |
| Jolles                     | 1953 | 1               | 50 : 50            |
| Freid, Lipman.<br>Jacobson | 1953 | 1               | 40 : 60            |
| Streil                     | 1954 |                 | 40 : 60            |
| Sopp, Stanton              | 1954 | 1.46            | 46 : 54            |
| Bruce, John                | 1954 | 1               | 40 : 60            |
| Cohen et al                | 1954 | 2               | 50 : 50            |
| Fervers                    | 1955 | 1.1             | 52 : 48            |
| Eichhorn Matschke          | 1956 | 1               | 39 : 61            |
| Pfeifer, Seidel            | 1956 | 1               | 40 : 60            |
| Kahr                       | 1956 | 0.65            | 40 : 60<br>30 : 70 |
| Becker, Kutting            | 1956 | 1               | 48 : 52            |

mental considerations, but from clinical experience. The only study on this problem is the paper by Barth, Schuba and Wachsmann<sup>7)</sup> (1957).

The present study investigates the problems of size of aperture, arrangement and area ratio.

### Arrangement

Various arrangements of sieve opening were considered. The most commonly employed sieve had perforations 1 cm in diameter, arranged in a square lattice with a distance of 1.4 cm between the centers of adjoining openings, permitting 40 per cent of a direct beam to pass; when the openings were arranged triangularly with the same interval, 46.2 per cent of a direct beam could pass.

In addition, as indicated in fig. 1, three types of sieve arrangement with a constant area ratio (50; 50), but various arrangements of openings were considered. One side of a square opening was 5 mm, and the whole sieve was 100 cm<sup>2</sup>.

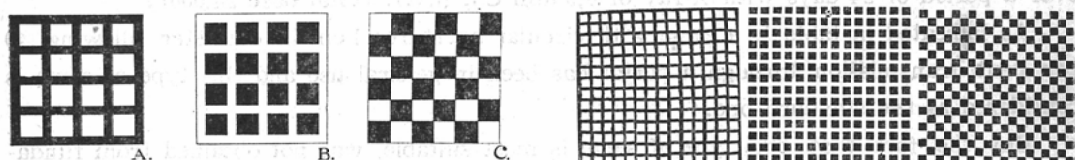


Fig. 1. Three types arrangement of sieves with a constant area ratio.

Used sieves of this experiment, one side of a square opening was 5 mm and the whole sieve was 100 cm<sup>2</sup>.

In the first experiment, 30 hybrid adult mice weighing 17 g were irradiated through a sieve with a single dose of 1,435 r in air under the following physical conditions: Voltage, 200 KV; current, 25 mA; filter, 0.7 mm Cu and 0.5 mm Al; distance, 40 cm and dose at a rate of 102 r per minute.

To avoid motion during irradiation, mice were narcotized with 5 cc per Kg of 10% solution of Urethan and placed in a wooden box 100 cm<sup>2</sup> in size.

The results of the first experiment are summarized in Fig. 2: with A type sieve the survival rate was 26.7% and with B type sieve 10%. In the second experiment, using three types of sieve, similar results were obtained: the survival rate of mice irradiated with the A or C type sieve was higher than with the B type sieve as indicated in Fig. 3.

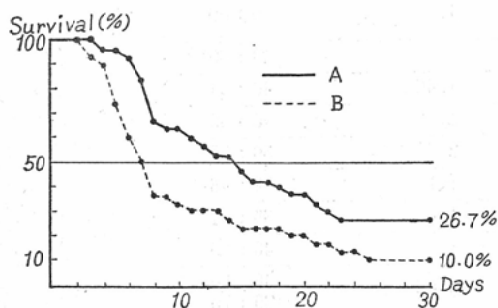


Fig. 2

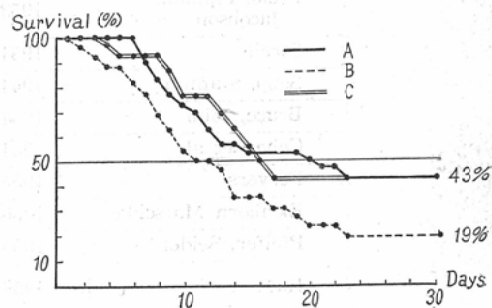


Fig. 3

These results show that as the covered areas are connected with each other in sieves of the A type, the diffusible substance produced in the irradiated area under the openings may diffuse from the circumferential covered area, and this dilution from diffusion will reduce the radiation effect under the openings. But with the B type sieve, which is the negative of the A type, each covered area is isolated and diffusible substance cannot escape. Thus, sieves of type A or C are more useful in reducing radiation injury to the skin.

#### Size of open area

As indicated in the previous paper by Kaneda and Kondo<sup>8,9)</sup>, with sieve plates with an area ratio of 40:60, the larger the size of opening is, the greater the injury to the vessels of rabbits' ears.

Similar results were reported by Kereiakes et al<sup>10)</sup>, who exposed rats to equal X-ray doses employing sieves with holes of various sizes, but with a constant area ratio: the survival rate rose as the size of the holes decreased, suggesting that survival rate is related directly to the area of interface between normal and irradiated tissue. The same results on skin were noted by Jolles<sup>11)</sup> (1953), Joyet<sup>12)</sup> and Hohl (1955), Vallebona and Bistolfi<sup>13)</sup> (1956), Seidel<sup>14)</sup> (1957), Schoen<sup>15)</sup> (1958), Barth, Schuba and Wachsmann (1958).

Jolles<sup>16)</sup> (1950) examined the reciprocal vicinity effect on the distance that diffusible substance travels, according to the size of irradiated areas on the upper half of the human thigh. He showed that for areas of 2.5 square cm. the hypothetical substance has no obvious effect beyond 2 cm. For areas of 6.25 square cm. it diffuses approximately 3 cm., and for areas of 12.5 square cm. it diffuses not less than 4 cm..

Kaneda and co-workers<sup>17)</sup> tried a similar experiment on the rabbit's ear to determine the range of interaction of diffusible substances histologically. Through two square openings of various sizes and at different distances from each other the rabbit's ear was irradiated with a single dose of 7,000 r, and 120 days later the skin at the middle point between the two openings was examined histologically. The minimum distances at which no pathological changes were seen in the hair follicles were:

| size of opening      | minimum distance |
|----------------------|------------------|
| 0.04 cm <sup>2</sup> | 0.1 cm           |
| 0.25 cm <sup>2</sup> | 0.42 cm          |
| 1 cm <sup>2</sup>    | 1.3 cm           |
| 2.25 cm <sup>2</sup> | 2 cm             |
| 4 cm <sup>2</sup>    | 3 cm             |
| 6.25 cm <sup>2</sup> | 4 cm             |

The effective distance of diffusible substance according to the size of an irradiated area is considered to be half these figures.

These results show that a fine sieve is suitable for the purpose of increasing the skin-tolerable dose, but the finer the sieve, the larger the scatter under the covered area until the dose distribution on the surface becomes almost uniform. Therefore a fine sieve cannot always be considered most suitable, and it is assumed that there is some limit to the size



of the openings.

Seidel<sup>18)</sup> (1959) examined the reaction of the human skin to irradiation, using a sieve of various sizes of openings, 1-10 mm in diameter and with 40 or 50% area ratio with repeated doses of 500 r to a total 10,000 r to the skin. He proved that the skin reaction with opening 2.5 mm in diameter was almost the same as with a coarse sieve, but with a fine sieve with 1 mm openings it was severe. Thus, with sieves of 40 or 50% open-area-ratio in order to obtain the greatest biological sieve effect with avoidance of severe skin injury, the minimum diameter of the openings is 2.5 mm.

#### Area ratio

Barth, Schuba and Wachsmann (1957) have been the only ones to undertake studies on the area ratio of a sieve. Using sieves with openings 8 mm in diameter and with various area ratios, they observed skin reactions in pigs irradiated with a single dose of 3,500 r and noted that the skin reaction decreased with the open-area-ratio; i.e. the lower the ratio, the less the biological sieve effect. And only when open-area-ratio was 25 per cent was increased skin reaction again observed.

However, in these studies, a uniform single dose was irradiated through sieves with various area ratio, so the volume dose was not the same in every case. In examining the biological sieve effect in animals, we must use the the same volume dose. There the authors undertook the following studies.

Through sieves all having openings 5 mm in diameter but with various area ratios, mice narcotized with Urethan were irradiated with the same volume dose. Total body irradiation of 600 r was given without a sieve, 3,000 r through a sieve with a 20:80 area-ratio; 2,000 r through one with a 30:70 ratio, 1,500 r through one with a 40:60 ratio; 1,200 r through one with a 50:50 ratio and 1,000 r through one with a 60:40 ratio.

The 30 day survival rate of these groups was compared. As indicated in table 2 and fig. 4, the larger the open-area-ratio, the lower the survival ratio. With a 60 per cent open sieve, the survival rate was lower than when no sieve was used, while a 50 per cent open area, or less, gave better results.

With a sieve with 20 per cent open area the following noteworthy results were obtained

Table 2. Survival ratio of mice after the irradiation with same volume dose through sieves with various area ratio.

| experiment | number of animals | area ratio    | air dose | survival after 30 days |            |
|------------|-------------------|---------------|----------|------------------------|------------|
|            |                   |               |          | number                 | percentage |
| 1          | 26                | without sieve | 0        | 26                     | 100        |
| 2          | 30                | 2 : 8         | 3000r    | 29                     | 96.7       |
| 3          | 30                | 3 : 7         | 2000r    | 20                     | 66.7       |
| 4          | 24                | 4 : 6         | 1500r    | 10                     | 41.7       |
| 5          | 30                | 5 : 5         | 1200r    | 10                     | 33.3       |
| 6          | 30                | 6 : 4         | 1000r    | 6                      | 20         |
| 7          | 27                | without sieve | 600r     | 6                      | 22.2       |

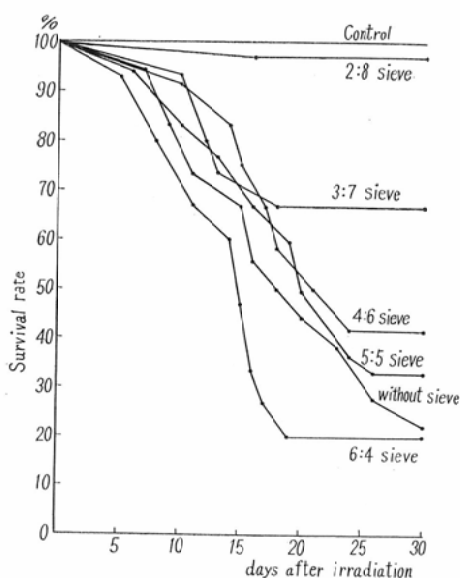


Fig. 4

as indicated in Fig. 6,; epilation occurred in areas directly under the openings, but even with a large dose of irradiation, the survival rate was 96.7 per cent, or almost the same as in non-irradiated controls.

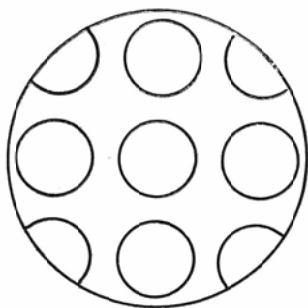


Fig. 5



Fig. 6

On the problem of whether or not to place a sieve in exactly the same position in successive irradiations.

Experiences with sieve therapy in our clinic suggest that the maximum tolerable human skin dose when sieve openings are placed in exactly the same position on successive irradiations is greater than when the sieve is moved from place to place. Nitta<sup>19)</sup> in our clinic tried to determine this relationship on the rabbit's ear with the following physical conditions using a Philips type tube: 45 KVp., 3 mA., distance 3 cm., field size 20 mm in dia-

meter, and dose rate 7,600 r per minute with a lead sieve of 1.5 mm in thickness and perforations 5 mm in diameter, arranged in a square lattice with a 40:60 area ratio.

With this sieve, five open areas and four half areas were included in a field 20 mm in diameter, as indicated in fig. 5. At the time of irradiation the rabbit was anesthetized with Rabonal to avoid movement. After 6-8 weeks, irradiation perforations of the ear were observed; the minimum perforation dose was deemed best for these observations.

The perforation doses with each irradiation method were:

Single irradiation

|                     |          |
|---------------------|----------|
| conventional method | 12,000 r |
| sieve method        | 80,000 r |

Fractional irradiation (5 treatments in 5 days)

|  |           |
|--|-----------|
| open areas placed exactly in the same position | 190,000 r |
| open areas in different positions              | 70,000 r  |

From these data, biological sieve effect ratios were obtained as indicated in table 3.

Table 3. Biological Sieve Effect Ratio

| Perforation dose with conventional method (M) | Position of open areas | Dose equivalent with sieve method |                | Biological sieve effect ratio (N/O) |
|---|------------------------|-----------------------------------|----------------|-------------------------------------|
|   |                        | physical (O)                      | biological (N) |                                     |
| 20,000r                                       | same                   | 50,000r                           | 190,000r       | 3.8                                 |
|   | diverse                | 50,000r                           | 70,000r        | 1.4                                 |

$$O = M/0.4$$

### Summary

Various experiments with sieves yielded the following conclusions:

1. The general clinical use of sieves with circular apertures 0.5-1 cm in diameter, allowing 40 or 50 per cent transmission through a portal was confirmed as most suitable by our experimental results.

2. From the technical standpoint, in sieves made of lead or lead-rubber, a square lattice arrangement is easier than a triangular one, although transmission through the latter is larger with the same minimum distance between centers of adjoining openings. Round openings are easier than square. When the open-area-ratio remains constant, the smaller the opening, the larger the dose that can be given to the human skin. However, technical and clinical conditions make the minimum practical size 5 mm in diameter.

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