



Example of refining and reduction (Project 82-02, Beckmann)

Observing rats using magnetic resonance imaging (MRI)

For several decades magnetic resonance imaging (MRI) has been used for diagnosis in medicine, e.g. to identify tumours. Nicolau Beckmann and his research team at the Novartis Institutes for BioMedical Research in Basle were able to demonstrate that this method is also useful in studies involving small laboratory animals for continually observing organs without any surgical intervention. The results are more expressive than those obtained using older methods where animals have to be sacrificed at each stage of the study. With Beckmann's method, up to 90% fewer animals are required, which is indeed a massive achievement with regard to the 3R principles.

A rat was placed in an MRI tube for around 10 minutes. The heartbeat was normal and the rat was breathing spontaneously, although it remained still because it had been temporarily anaesthetised using gas. In this way the MRI could record precisely the interaction between the hydrogen nuclei in the rat's body and the strong magnetic field, as well as high-frequency radio waves. The MRI machine produced images from these signals, providing information about the organs within the rat without any surgical intervention. The rat had fully recovered from the anaesthetic ten minutes after the end of the test.

The animals used in this test had an artificially induced pulmonary inflammation and were thus a "model" for diseases of the airways. As a result of the inflammation, fluid had collected in the lung tissue which produced a signal that the MRI could pick up. A number of animals were not treated and in these cases the inflammation began to heal naturally; the signals picked up by the MRI gradually decreased. In another group of animals, once the inflammation had become apparent, a single dose of a drug with a possible anti-inflammatory effect was given. In the case of one of the drugs tested by Nicolau Beckmann, the effect was rapid and marked – within hours the signals picked up by the MRI had decreased considerably. This meant that the drug in question may well be of interest for treating pulmonary inflammation in humans.

With the conventional method of lung lavage in dead animals it has never been possible to obtain such accurate results. In particular it has not been possible to time the processes with such precision in one and the same animal.

It must be said that the changes observed using MRI provide only a general indication of what happened in the lung model; they did not show for example the biochemical or cytological processes that resulted in the visible changes. Nevertheless, the MRI method provided statistically sound evidence that a certain drug had a desired effect. This information was obtained through tests that used only a fraction of the number of animals that would have to have been sacrificed using a conventional method, and the animals used were subjected to only a minimum of discomfort. This is indeed an important achievement with regard to the 3R principles.

http://www.forschung3r.ch/en/projects/pr_82_02.html

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20 November 2012

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