# Subcutaneous Versus Intraperitoneal Placement of Radiotelemetry Transmitters for Long-term Recording of Electroencephalography.

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H. Lundbeck has been one of the pioneers in the use of implantable radiotelemetry devices for the collection of electroencephalographic (EEG) and electromyographic (EMG) data in rats. This technology is useful both for sleep research (Vogel et al., 2002: J. Neurosci. Methods *118*, 89-96) and epilepsy research (Bastlund et al., 2004 J. Neurosci. Methods *138*, 65-72). As part of an ongoing process to improve the ethical and technical aspects of our animal models with focus on the 3R's, we are engaged in continuous dialogue with our in-house veterinary staff, the equipment manufacturers and other research groups using the telemetry technology. At Lundbeck, we had formerly been implanting the transmitter devices in the intraperitoneal (IP) cavity, however, we were experiencing a number of difficulties with this method. For example, this procedure requires multiple incisions as well as turning the rat over during surgery, compromising the aseptic conditions and thereby increasing the risk of infection. Past experience with subcutaneous (SC) implantation revealed that this technique may also lead to infection, seromas and in some cases penetration of the leads and/or the transmitter body through the skin. However we have further developed our surgical procedure for the SC implantation, optimising and focusing on aseptic surgery without compromising the quality of the data.

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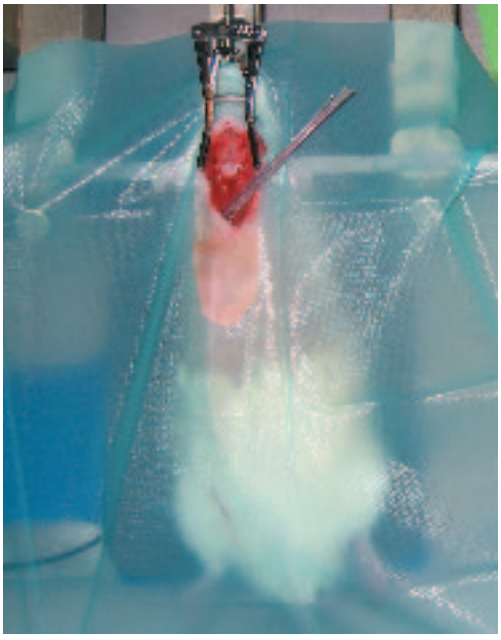

Figure 1: Rat fixed in a stereotaxic frame with aseptic operation covers and sterile instruments.

We use 300-400 g male Sprague Dawley rats for SC implantation of TL10M3-F50-EET/EEE radiotelemetry transmitters (Data Science International, USA). All rats are treated with prophylactic antibiotic and peripherally acting analgesia 15 minutes prior to surgery by injection of 5 mg/kg Baytril® vet. (SC, enrofloxacin, Bayer, Germany) and 1.5 mg/kg Rimadyl® vet. (SC, carprofen, Pfizer, USA), respectively. Rats are anesthetised with a 0.2 ml/100g (SC) injection of one part Hypnorm® (0.315 mg/ml fentanyl + 10 mg/ml fluanisone, Jassen Inc., USA) one part

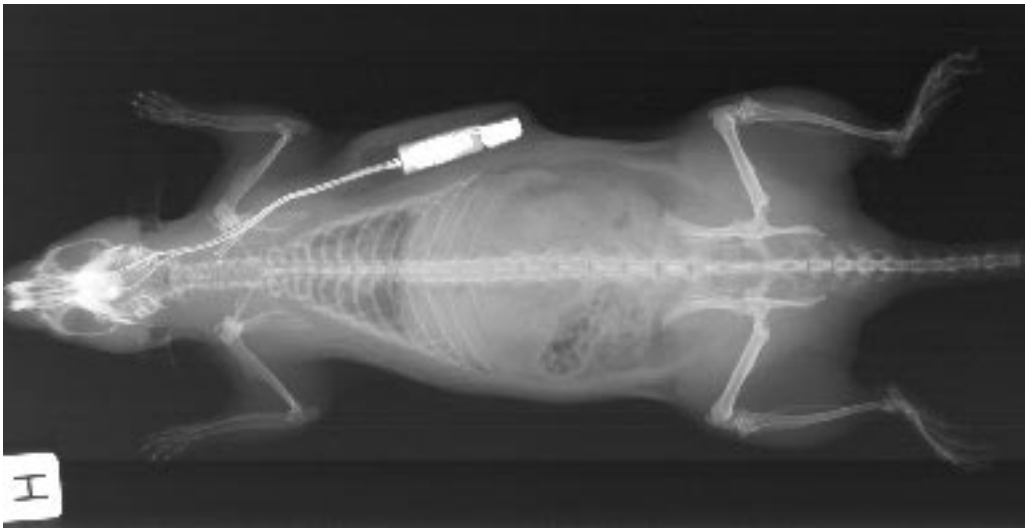

Figure 2: X-ray of a rat implanted with a TL10M3-F50-EET subcutaneously.

Dormicom® (5 mg/ml midazolam, F. Hoffmann-La Roche AG, Switzerland) in two parts sterilised water.

The rat is clipped from the nose down to the tail, swabbed with iodine and placed in a stereotaxic frame. The rat is covered with a sterile operation cover and the incision area from the nose to between the shoulders is exposed. Sterilised surgical instruments are then placed on a sterile operation cover. We place the body of the transmitter in a SC pocket on the back of the rat's hind flank. The EMG electrodes are placed bilaterally in the neck muscle (musculus cervicoauricularis) and EEG electrodes supradurally in bore holes in the skull (for detailed description see Bastlund et al., 2004). After surgery, animals are given centrally acting pain relief by injecting 0.1 mg/kg Temgesic® (buprenofin, Schering-Plough, USA) and placed under warming lamps until recovery of consciousness. Rats are treated with Rimadyl® and Baytril® for 6 days and after 7-10 days the sutures are removed. The rats are closely observed during a 14-day post surgical recovery period and treated with Xylocain® cream where required to avoid irritation around the wound.

We see no inflammation around the body of the transmitter or SC leads post surgery, resulting in a fuller and faster recovery than that seen with IP implantation. After SC implantation the rats regain normal exploratory activity after 1-2 days compared with 4-5 days after IP placement. A few animals develop seromas around the transmitter but these disappear harmlessly without intervention after 2-3 weeks. In our experience, we are able to maintain implanted rats for over 3 months with only minimal incidence of leads and/or transmitters penetrating the skin. Furthermore, the surgical procedure for SC implantation is faster and less complicated to perform, thus surgery time is reduced from $1^{1}/_{2}$ hours to 45 minutes. With the SC implantation it is easier to work aseptically and keep the rat fixed in the stereotaxic frame throughout the procedure, hence maintaining a sterile work area.

In conclusion, we believe that the techniques outlined here offer significant improvements in terms of both animal usage and welfare, as well as optimising the overall throughput of the surgical procedure and not compromising the data quality.