

**Excerpt from "Microchip-Induced Tumors in Laboratory Rodents and Dogs: A Review of the Literature 1990–2006"**

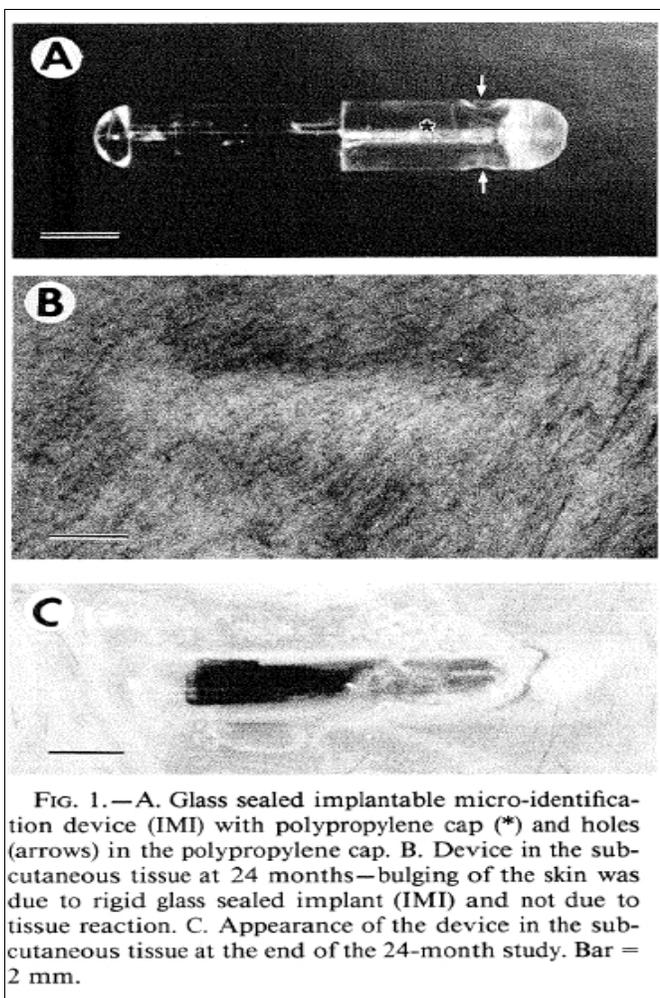
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**Rao & Edmondson, 1990**

Tissue reaction to an implantable identification device in mice. *Toxicologic Pathology*. 1990;18(3):412–416.

Author(s)	Species	# of Animals	Length of Microchip Exposure	Developed Cancer
Rao & Edmondson, 1990	mice	10	3 months	none observed
		10	15 months	
		74	2 years	
		39	Less than 2 years	



**Summary of Study**

140 mice were implanted with subcutaneous microchips and evaluated for adverse reactions. The tissue surrounding the implants was examined after periods ranging from three months to two years. No neoplastic (abnormal tissue growth) reactions were observed.

**Study design and key findings**

The study was published in 1990, at a time when implantable microchips were first being introduced to laboratories for animal identification purposes.

The goal of the project was to "determine the tissue reaction [from the implant], especially its potential to cause subcutaneous sarcoma, and the stability and reliability of a glass-sealed permanent identification device" implanted in mice. (p. 412 – 413)

Researchers implanted 140 B6C3F1 mice with a microchip at approximately six weeks of age. Ten mice of each sex were evaluated at 3 months and at 15 months. The remaining animals were evaluated at 24 months.

Histologic examination presented a connective tissue capsule of variable thickness around most of the implants, especially in the area of the glass surface of the chips. Around the polypropylene cap of the transponder, inflammatory reactions were detected but no neoplasms observed.<sup>1</sup>

1 From a summary of the Rao & Edmondson study included in Tillmann et al. (1996), p. 200.

The following chart shows the length of time each subgroup of mice was exposed to the microchip implant before being evaluated.

# of Mice	Length of Implant Exposure
10	3 months
10	15 months
74	2 years
39 <sup>2</sup>	Less than 2 years (evaluated prior to study conclusion due to death of the animals)
7	Transponder lost or failed

The capsule that formed around the polypropylene cap of the device contained minimal to mild inflammatory reaction with lymphocytes, macrophages, and a few plasma cells and neutrophils. "Chronic granulomatous inflammation . . . was also observed around the polypropylene cap of 2 implants." (p. 414)

Though no cancer was found, there were other problems with the implants. According the researchers, two of the implants were "lost" and four of the devices "failed." Three of these failures were attributed to microscopic cracks in the weld connecting the antenna leads to the microchip, and one was caused by "leakage of the glass capsule resulting in fluid accumulation around the microchip." (p. 413) One device lodged in the subcutaneous tissue over the lumbar vertebrae and was pushed out slowly through the scar tissue of the injection site during the tenth month of the study.

In addition to the lost or failed transponders, seven of the transponders were discovered in the abdominal cavity of the animals rather than in the subcutaneous tissue where they should have been located. Researchers did not know whether the devices had migrated into the abdominal cavity and eventually fixed in the perirenal tissue, or whether lab technicians had accidentally injected the devices into the abdomen.

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### Concern over the Design and Statistical Validity of the Study

Given the small sample of animals exposed to the microchip for a full two years, this study may suffer from similar statistical validity problems as the Murasugi et al. (2003) and Ball et al. (1991) studies discussed above.

Tillmann et al. (1997) point out this deficiency in their writeup, stating that the lack of tumor findings by Rao and Edmondson could be explained "by the low number of 140 B6C3F1 mice used by Rao and Edmondson." (p. 200).

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### Study Details

- The study was conducted by Ghanta Rao and Jennifer Edmondson at the Division of Toxicology Research and Testing at the National Institute of Environmental Health Sciences National Toxicology Program in North Carolina.

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2 This figure is inferred from the following statements: "Survival at the end of the 24-month study was 74% and 70% for the male and female mice respectively" (p. 413) and "Mice that died during the course of the study...were necropsied...and evaluated by light microscopy for tissue reaction around the device." (p. 413)

- Animals used were B6C3F1 mice.
  - Microchips used were obtained from BioMedic Data Systems, Inc. They were described as "a glass sealed 12 x 2 mm cylindrical device with a snug-fit biocompatible polypropylene cap covering a 5 mm length of the device. There are two holes in the polypropylene cap. The purpose of the polypropylene cap is to elicit mild tissue reaction and immobilize the device at the site of the implantation." (p. 413).
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