
Long-Term Health Effects of Embedded Depleted Uranium

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Disclaimer

The views expressed in this presentation are those of the author and do not reflect the official policy or position of the Armed Forces Radiobiology Research Institute, the Uniformed Services University, the Department of Defense, or the United States Government.

The Embedded Pellet Rat Model

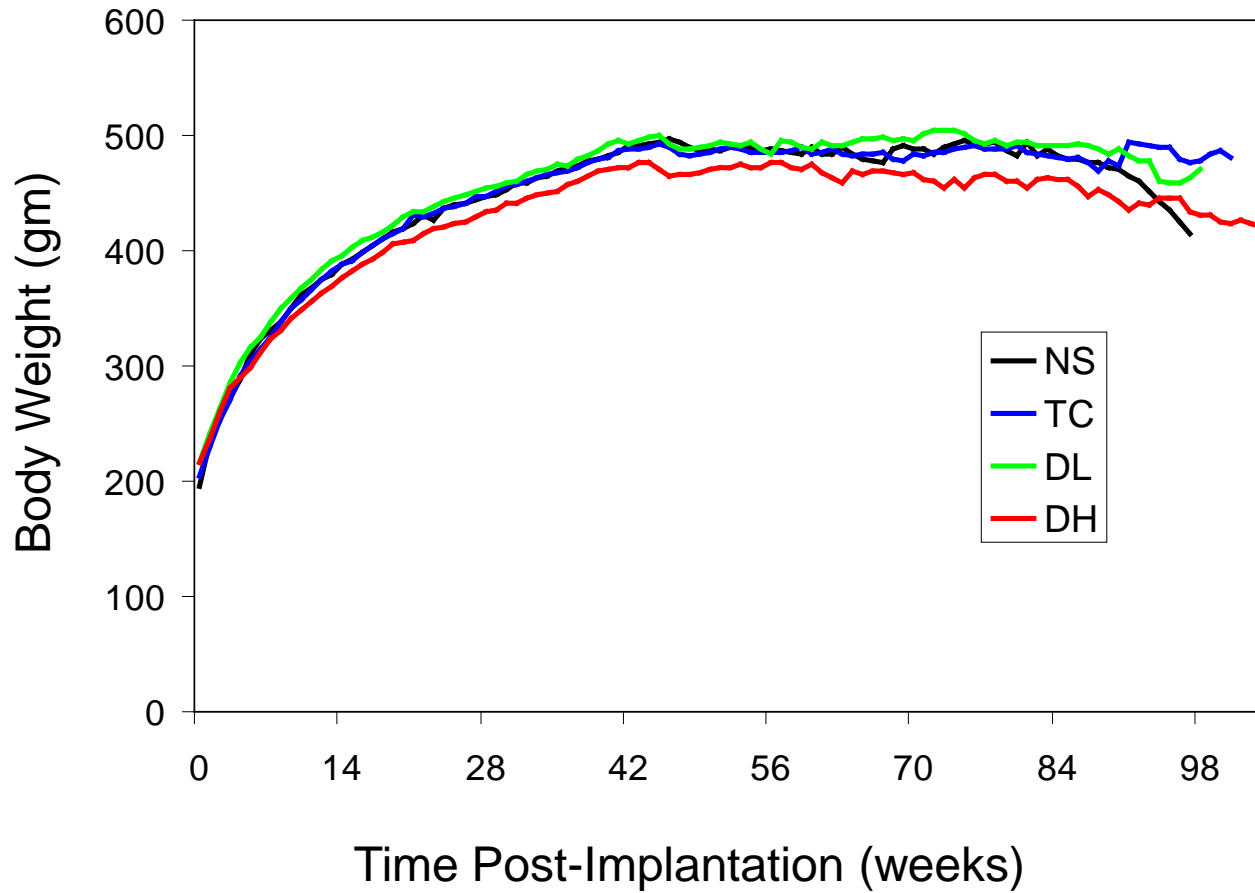


X-ray of pellets implanted in gastrocnemius muscle

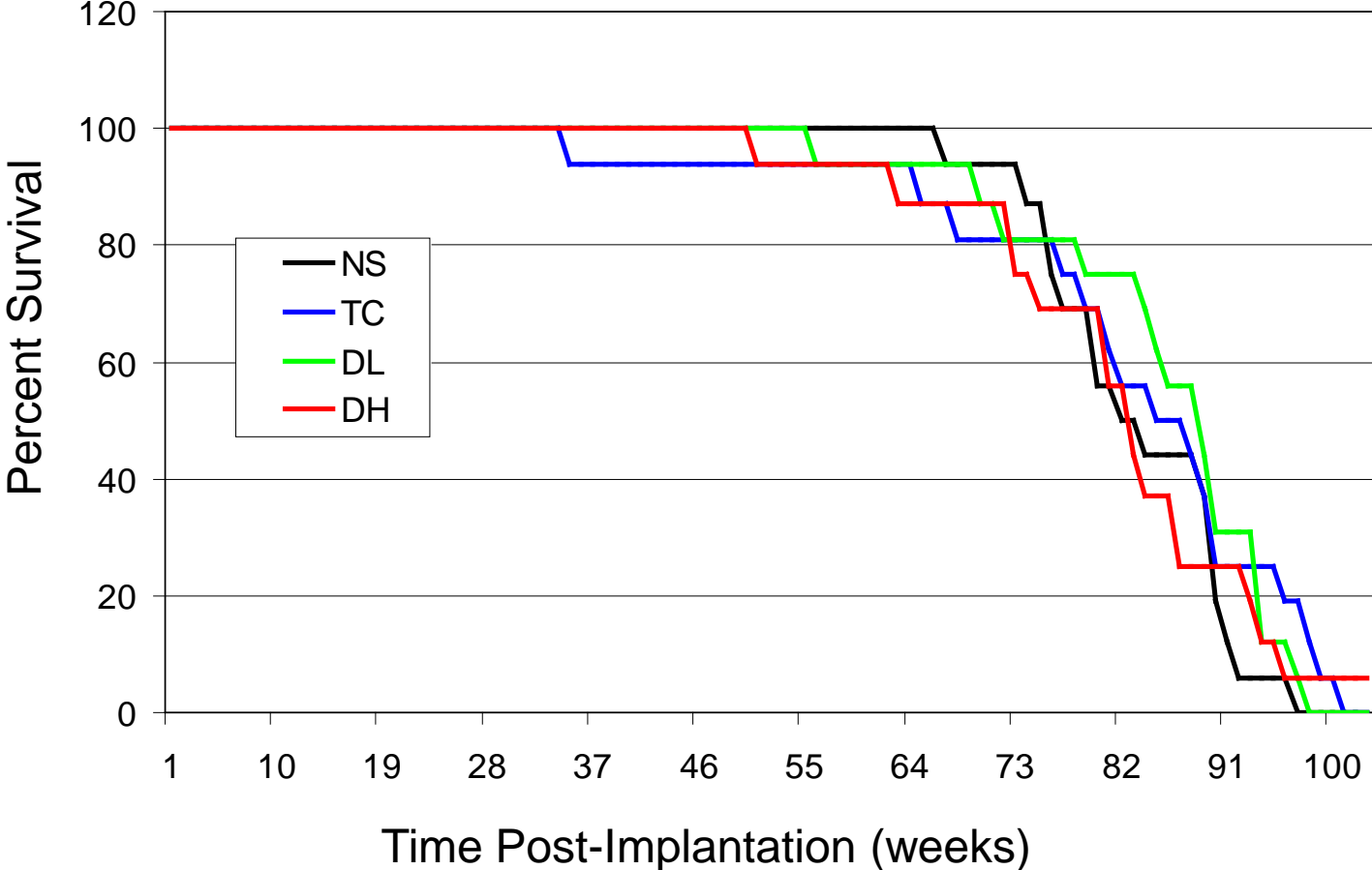
Experimental Approach

- Two-year longevity study to determine whether intramuscularly implanted DU or tungsten alloy pellets are carcinogenic.
- Six treatment groups of Fisher 344 rats
 - **Two groups with 4 or 20 DU pellets**
 - Two groups with 4 or 20 tungsten alloy pellets (91% W, 6% Ni, 3% Co)
 - One nickel group (positive control)
 - One tantalum group (negative control)
- One set of pellet-implanted rats for duration of study. Second set includes rats euthanized at selected times after pellet implantation to provide tissues for histopathology, assessment for metal content and immunotoxicity testing.
- USAMRMC Award DAMD17-01-1-0821

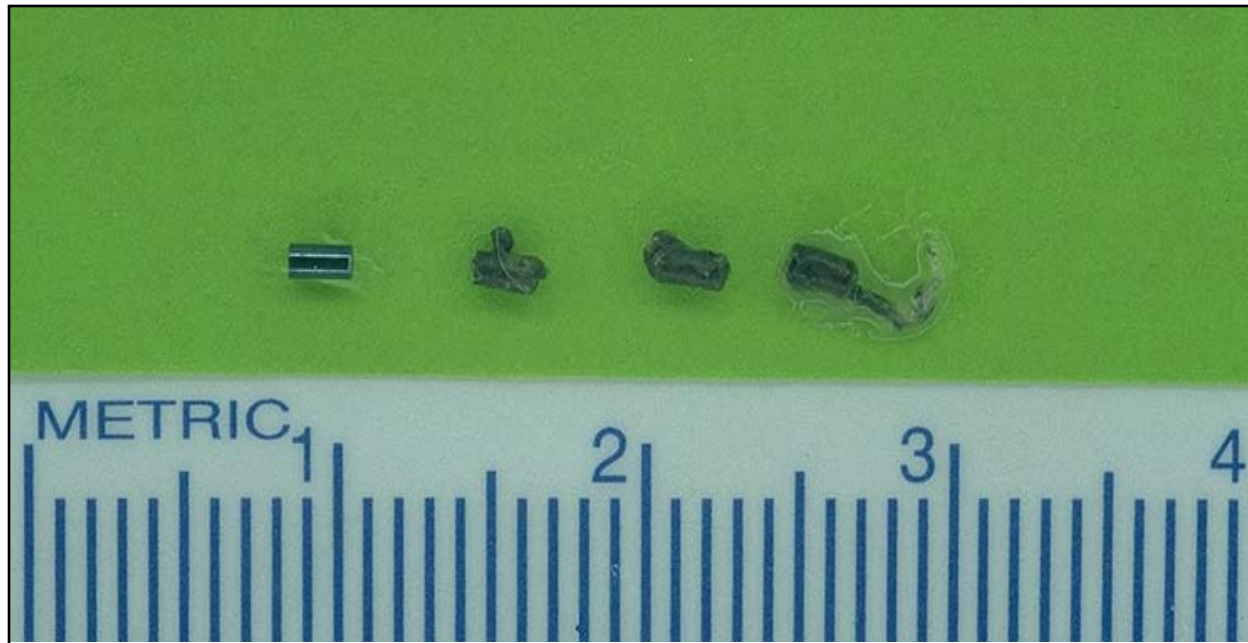
Body Weight Gain After Pellet Implantation



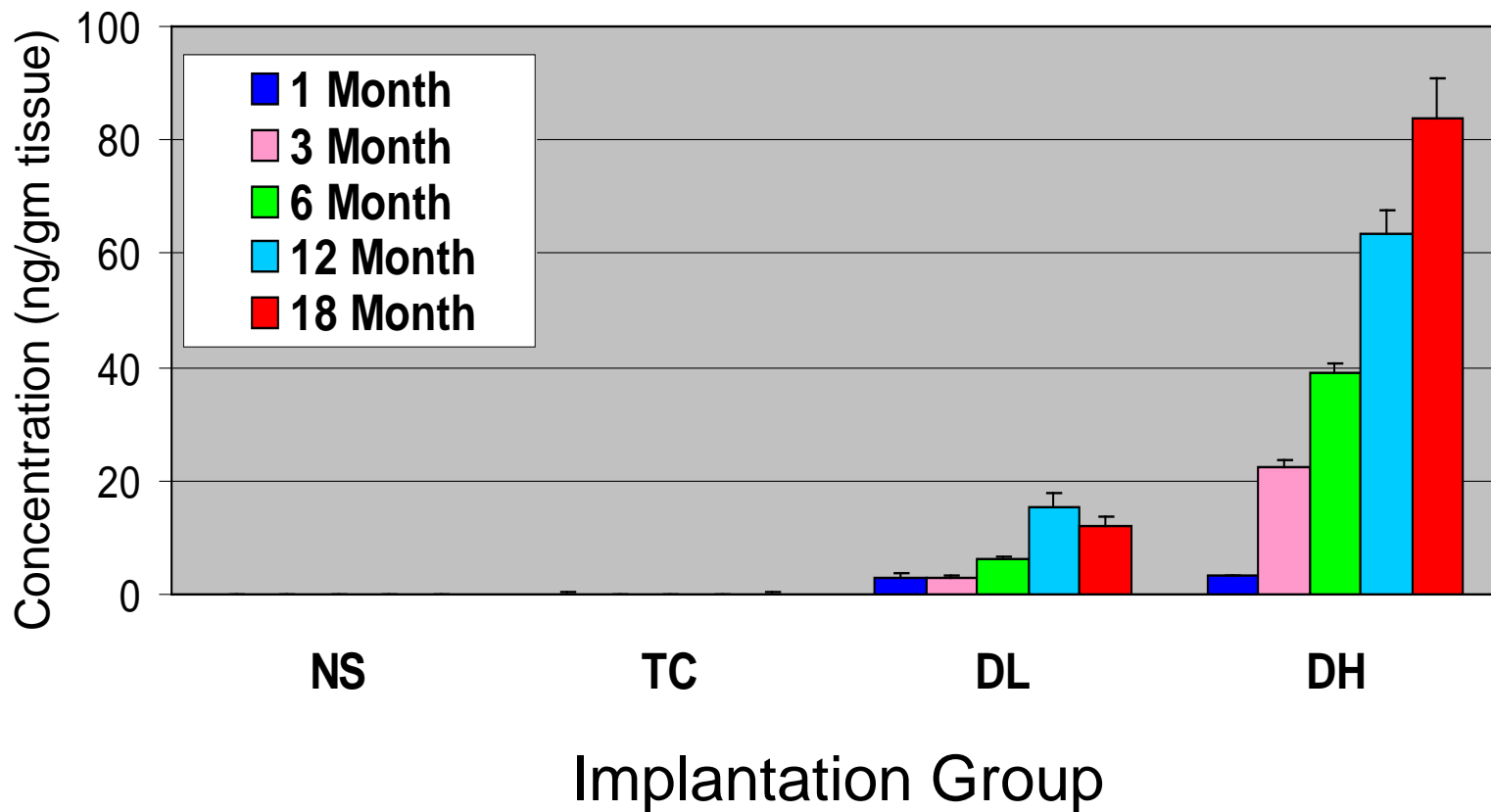
Survival After Pellet Implantation



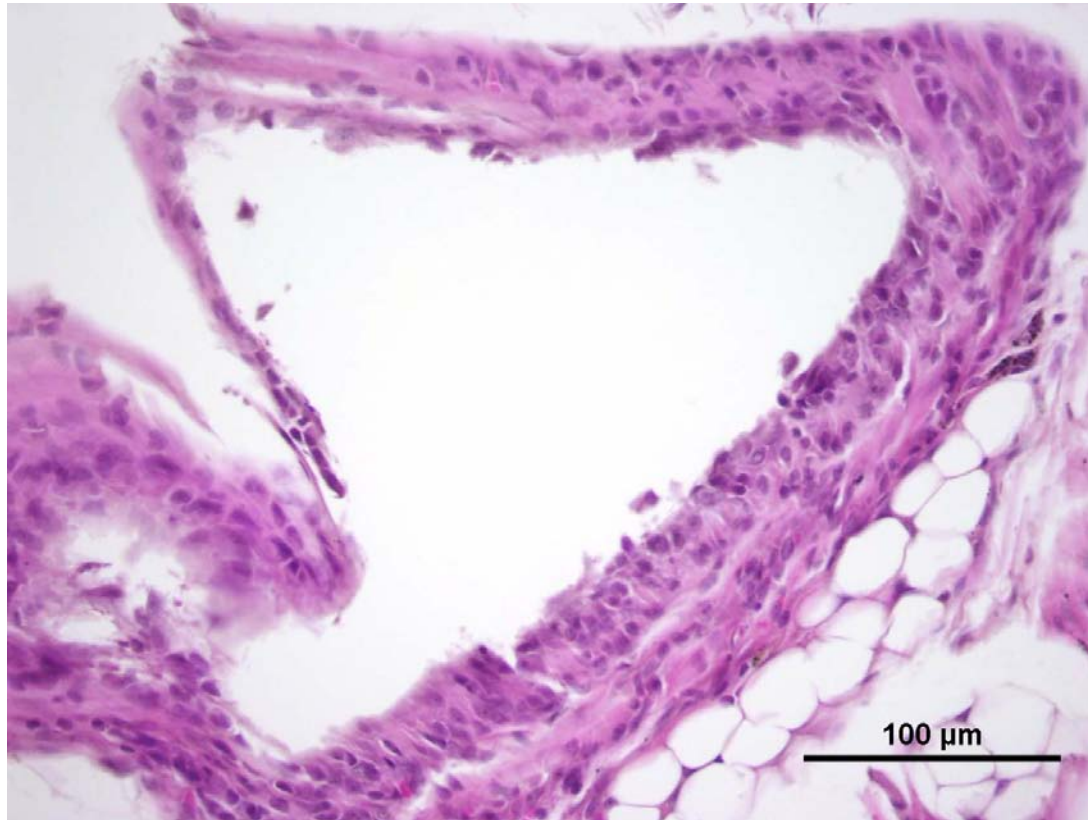
DU pellet implants: new and 12 weeks



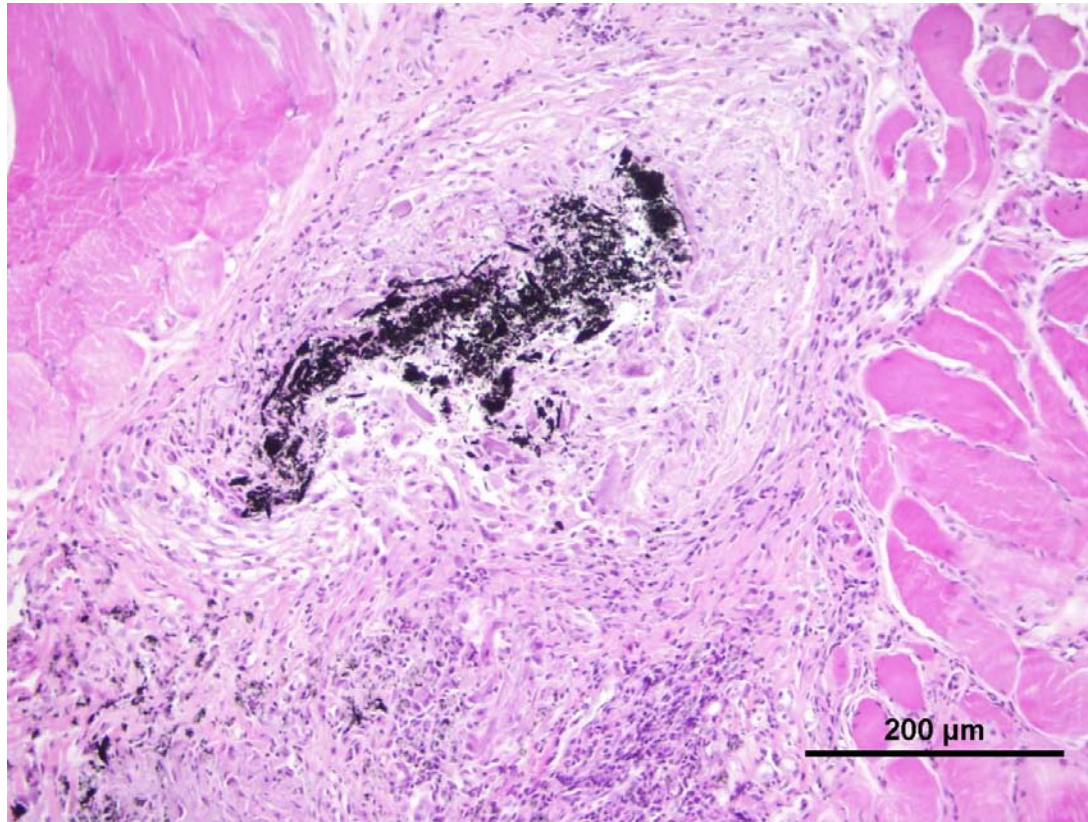
Spleen Uranium Levels



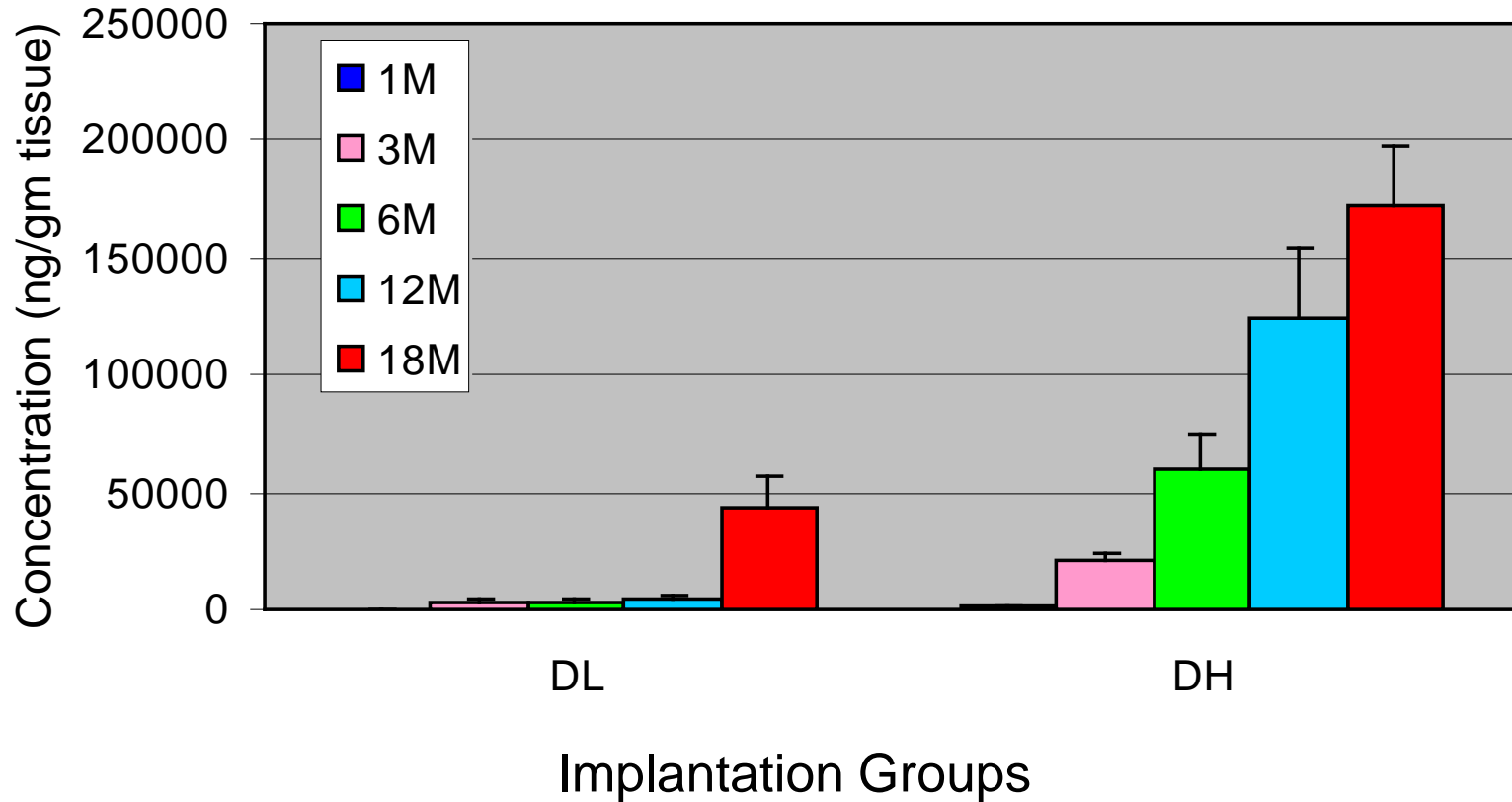
Fibrotic Capsule from DU Implantation Site (13 weeks)



DU Implantation Site – 13 weeks



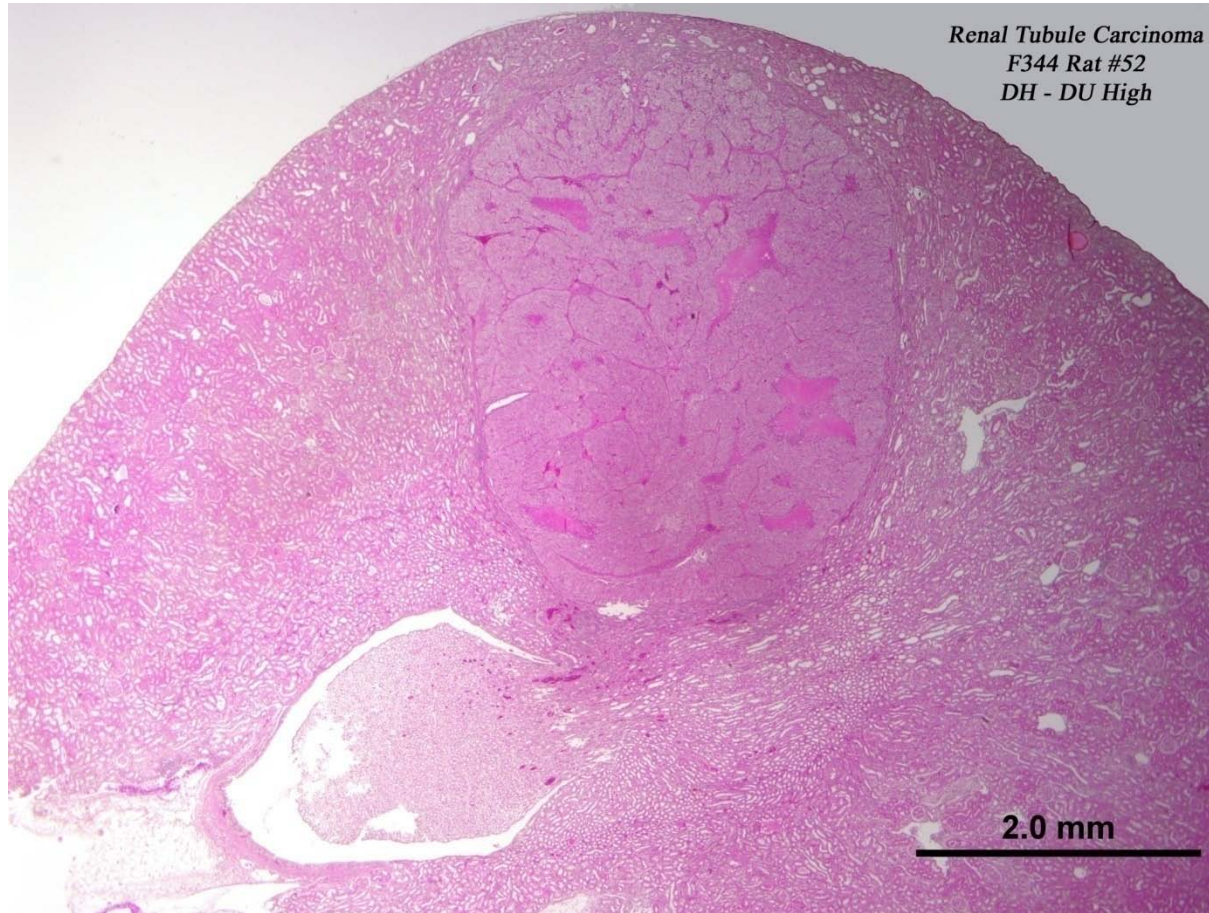
Popliteal Lymph Node Uranium Levels



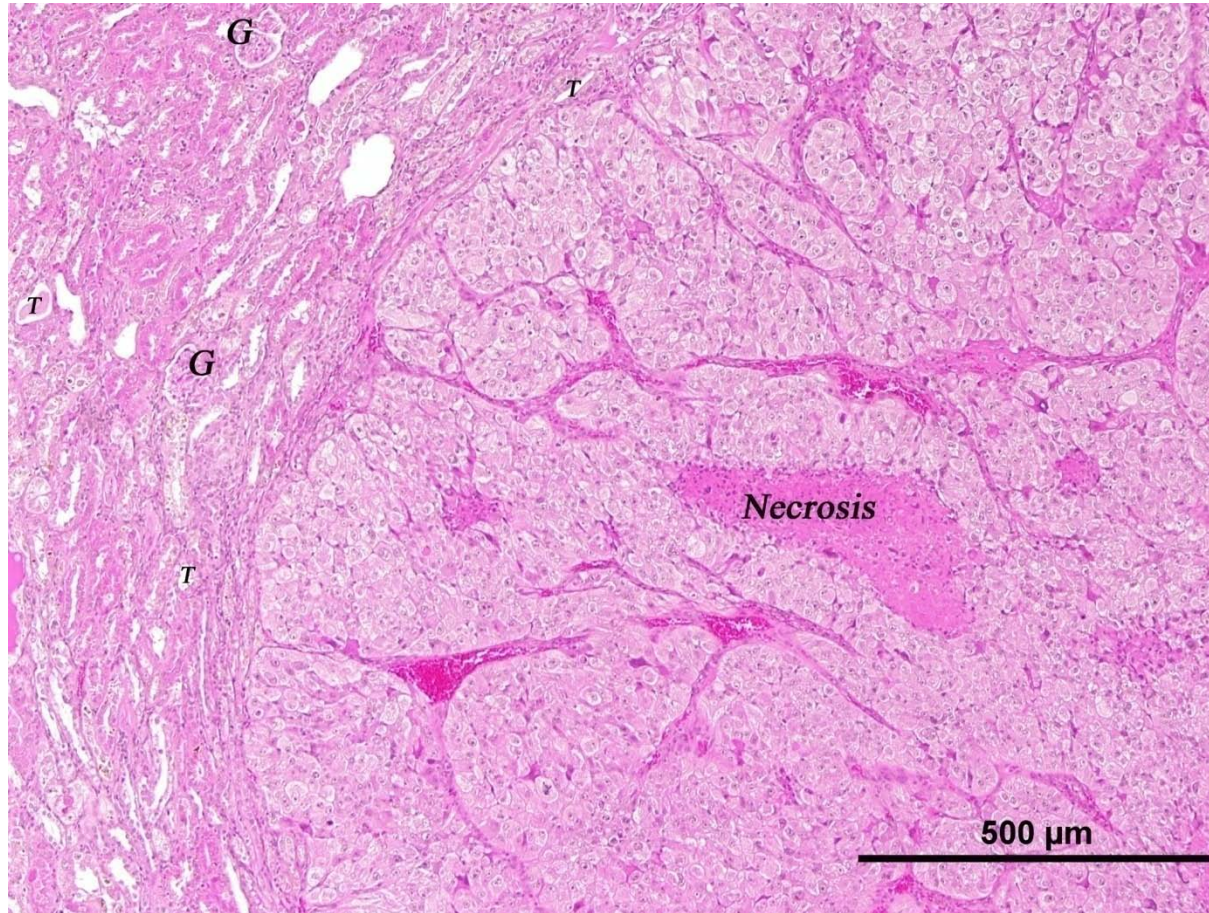
Tumor Distribution Based on Gross Necropsy Examination

	6 Month (n = 20)	12 Month (n = 20)	18 Month (n = 10)	24 Month (n = 16)
Non-surgical	None	1-abdominal	8-testicle	7-testicle 3-abdominal
Tantalum	2-abdominal	None	8-testicle 2-abdominal	9-testicle 5-abdominal 1-muscle (leg)
DU Low Dose	None	2-abdominal	8-testicle 1-abdominal	10-testicle 1-abdominal 1-adrenal 1-kidney
DU High Dose	None	2-abdominal 1-lung	6-testicle 2-abdominal 1-kidney	9-testicle 2-lung 8-kidney 1-muscle (leg)

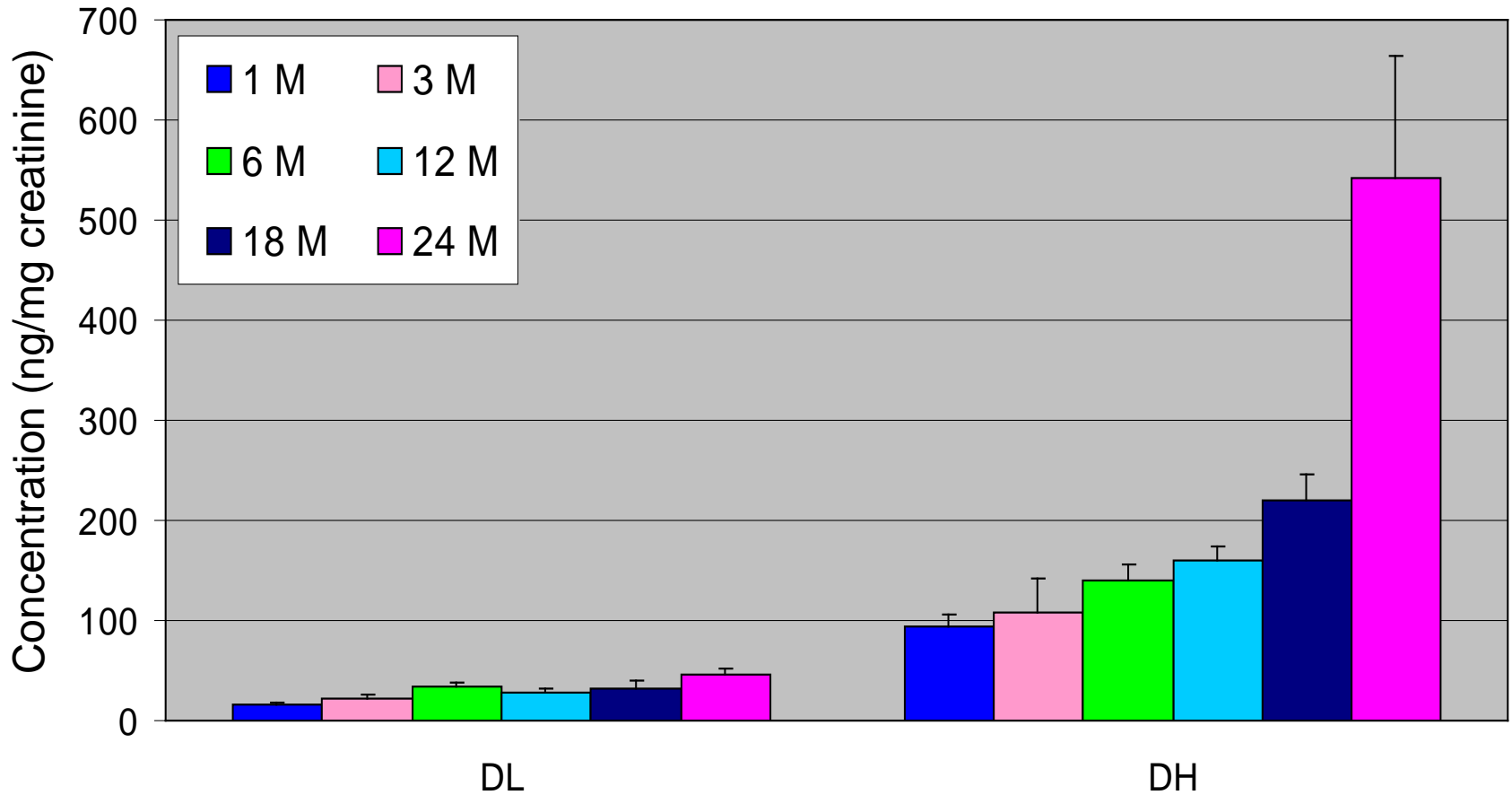
Renal Tubule Carcinoma – High-Dose DU (104 weeks)



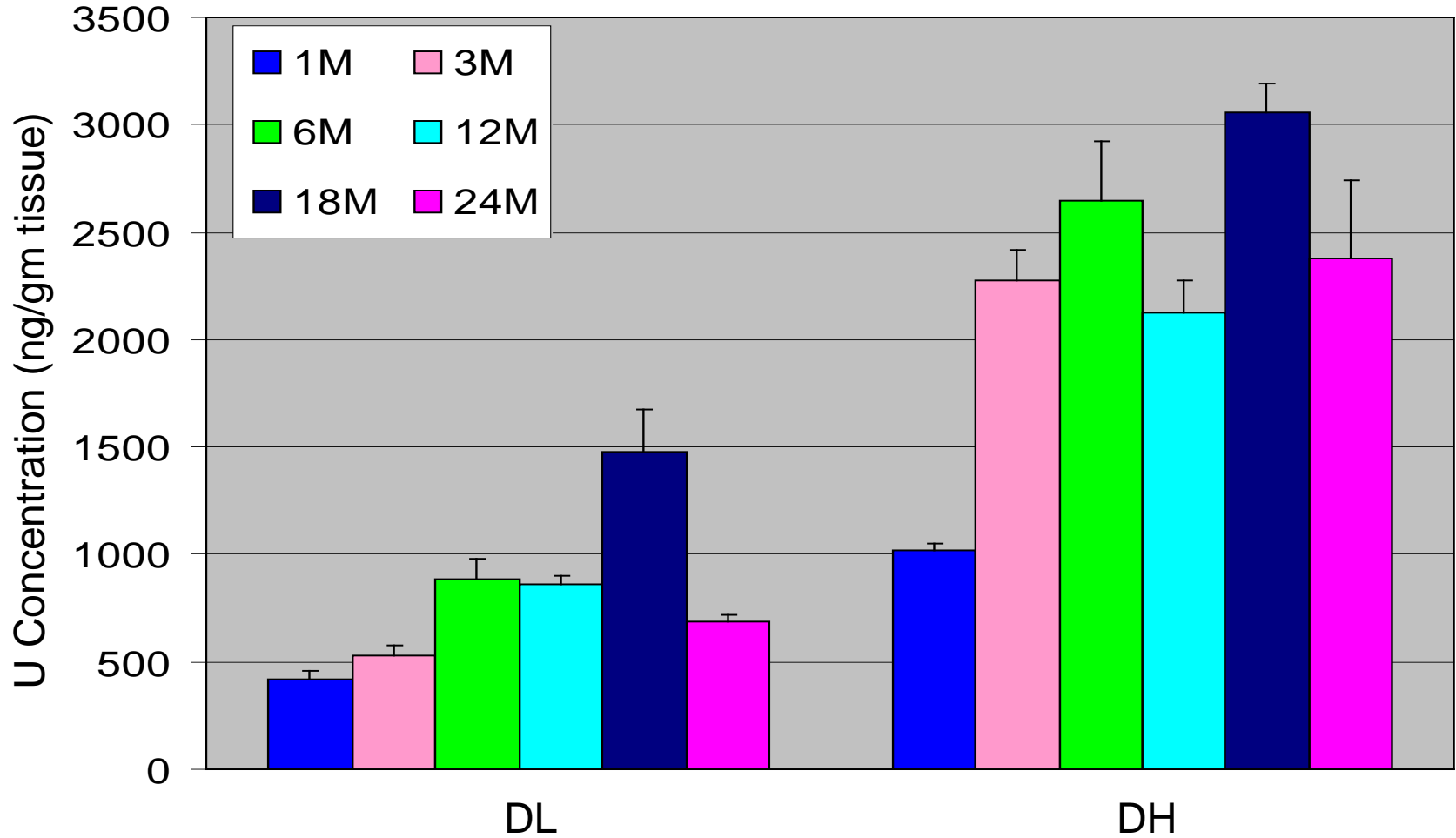
Renal Tubule Carcinoma – High-Dose DU (104 weeks)



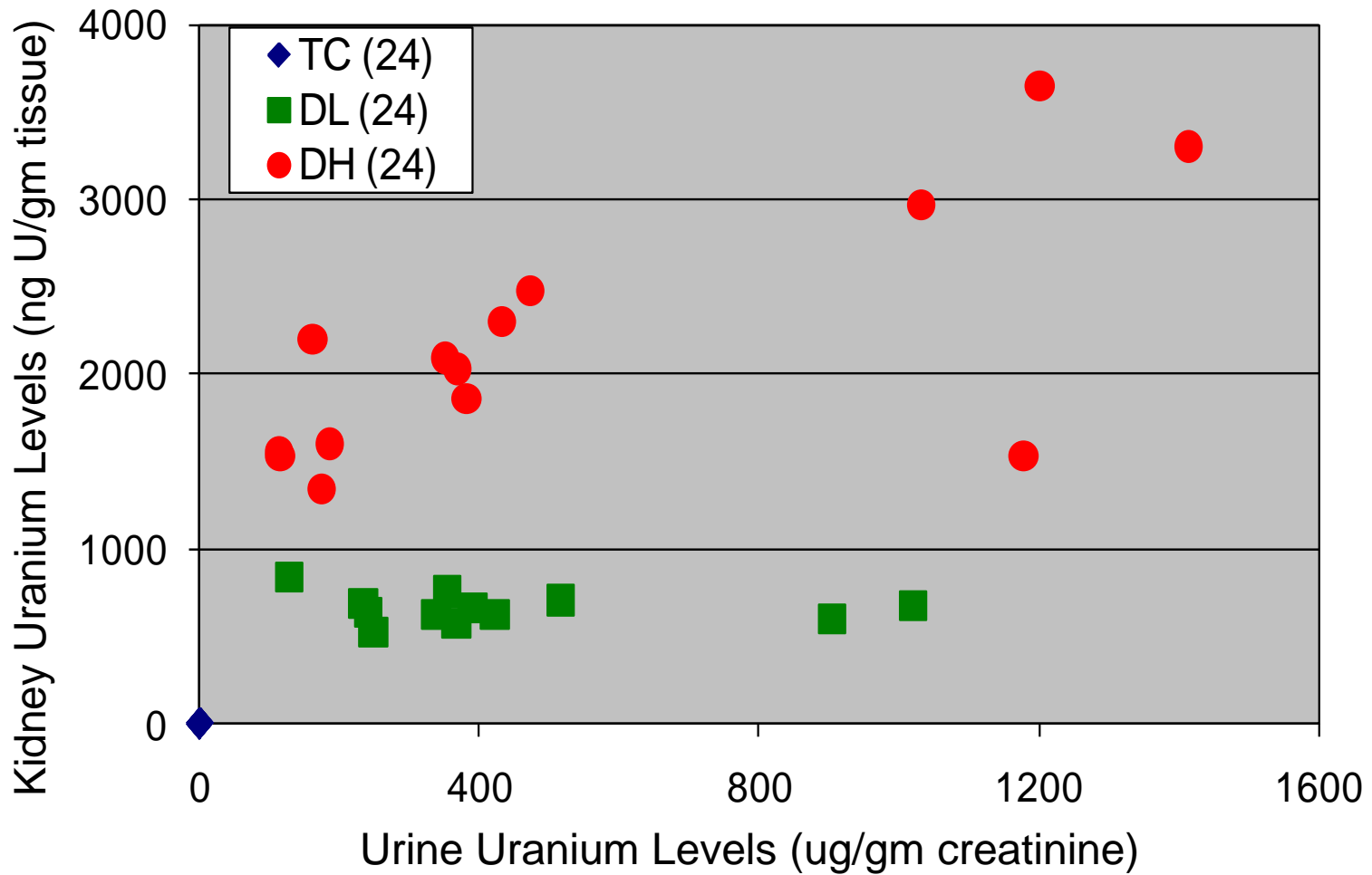
Urine Uranium Levels



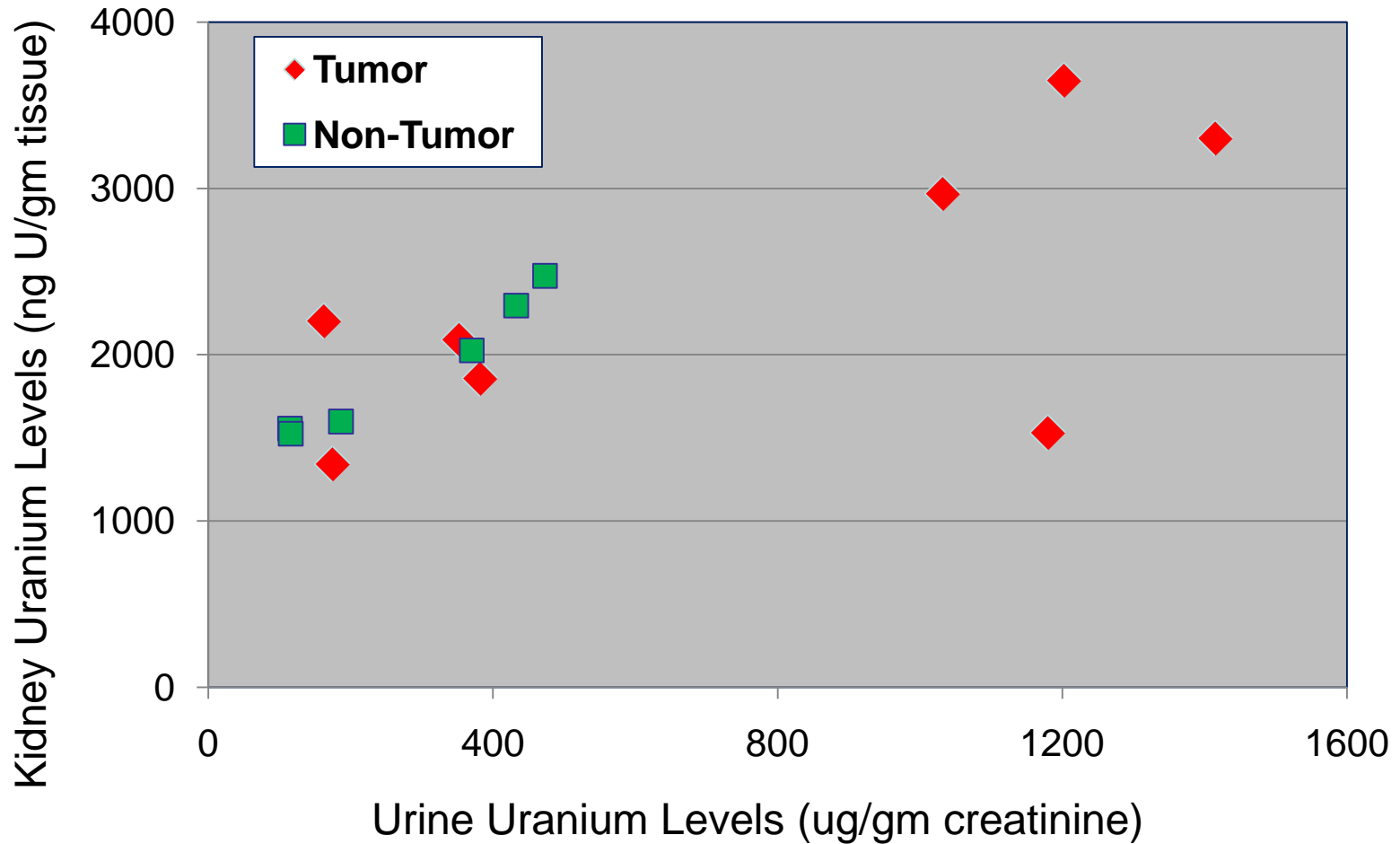
Kidney Uranium Levels



Correlation of Kidney and Urinary Uranium Levels



Uranium Levels in Rats with and without Renal Tumors



Summary

- DU-implanted rats did not exhibit tumors at the pellet implantation sites.
- High-dose DU rats, in the 24 month group, had an increased incidence of renal neoplasias.
- Urine uranium levels in DU-implanted rats increased over time in a dose-dependent manner.
- Uranium levels in the kidney also increased over time, reaching 3 $\mu\text{g/g}$ tissue by 18 months in the high-dose DU group.

Current Work

- Continue histopathology assessment of renal carcinomas

Future Directions

- Identify early serum or urinary biomarkers of DU-induced neoplastic renal changes
- Investigate molecular mechanisms associated with DU-induced renal effects
- Tier-testing approach for assessing potential health effects of embedded metal fragments

The “Team”

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QUESTIONS

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