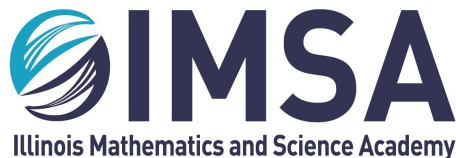


# Diagnostic $A\beta$ O-targeted probes for Alzheimer's Disease

Nafay Abdul and Sophia Pribus

*Advisers: Kirsten Viola, William Klein*

*Collaborators: Vikas Nandwana, Rohan Chalasani, Adrian Bebenek, E. Alexandria Waters,  
Nicholas Rozema, Craig Weiss*

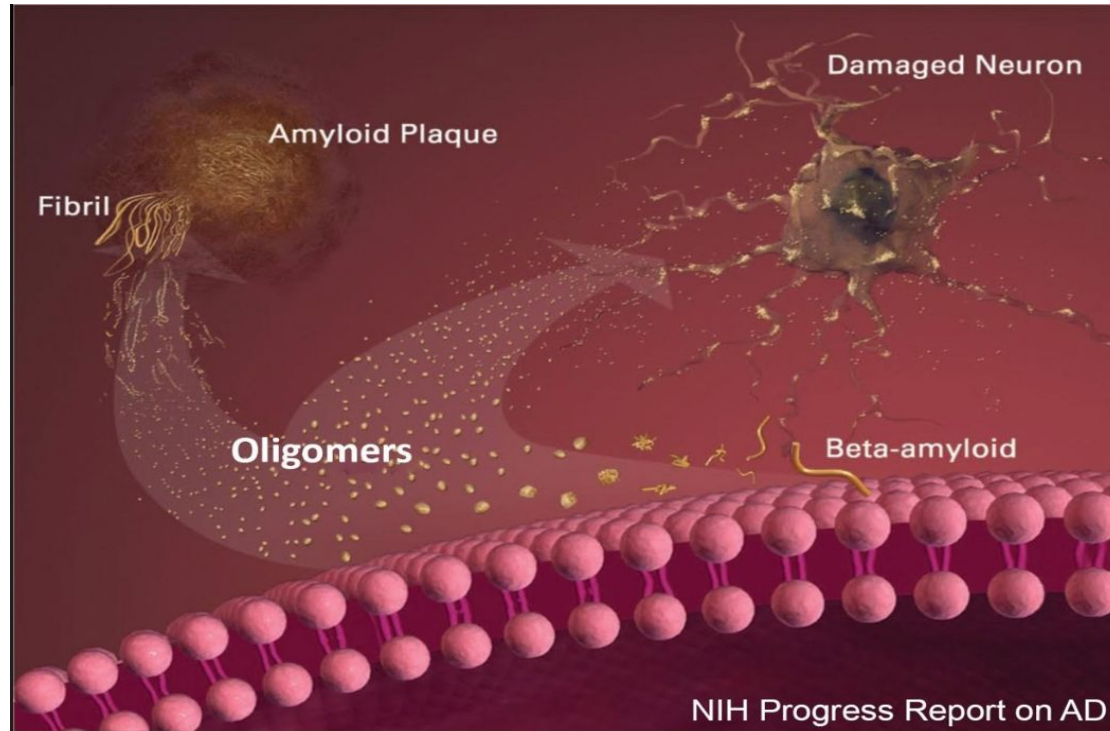


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# Alzheimer's Disease

- 1 person develops AD every 65 seconds
- treatment cost US \$277 billion in 2018
- plaques and tangles develop between nerves and inside cells
- symptoms: memory loss, confusion, difficulty speaking, swallowing and walking

# A $\beta$ oligomers vs Fibrillar Amyloids



# A $\beta$ Hypothesis

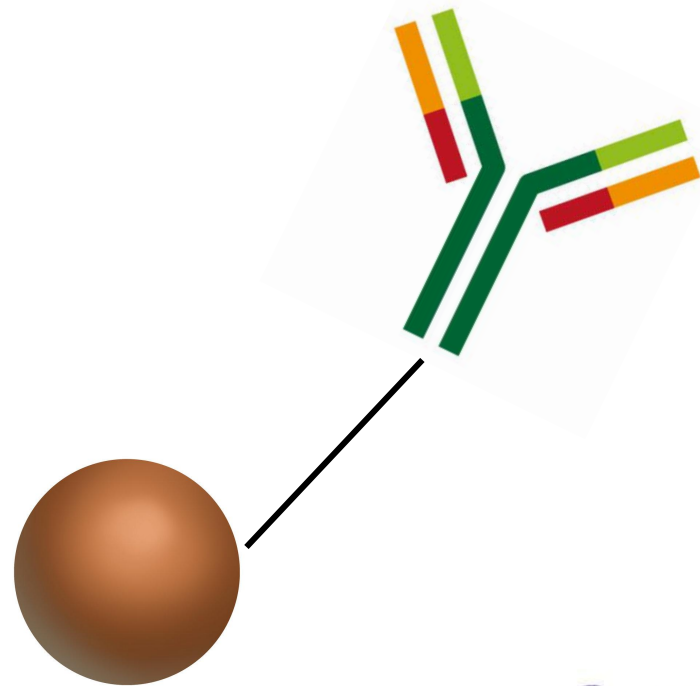
The accumulation and deposition of oligomeric or fibrillar amyloid  $\beta$  (A $\beta$ ) peptide is the primary cause of Alzheimer's disease (AD)

# Current AD Diagnostics

- **MRI** → used to quantify brain volume/measure brain metabolism
- **Probes** → used to target certain structures for imaging
  - e.g. PET probes → quantify ThioS-positive amyloid plaques
  - No probe specifically for AβOs

# A $\beta$ Probe

- Attach oligomer-specific antibodies onto magnetic nanostructures
- Binds to A $\beta$  oligomers to give a magnetic resonance imaging signal



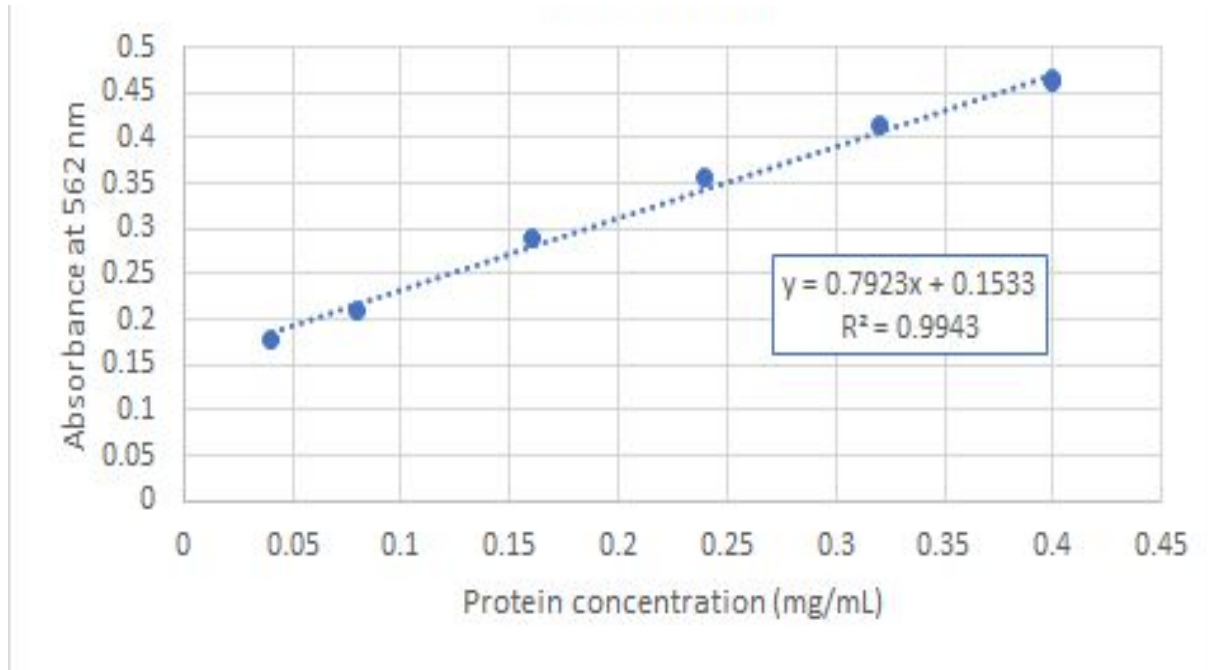
# Methodology

- Protein assays
  - testing and improving conjugation efficiency of MNS to antibodies
  - optimal method - double conjugation method
- In vivo testing
  - mouse model
  - rabbit model
- Immunohistology
  - sliced brain cells
  - immunofluorescent

# Probe Development Data



# Absorbance of Standards



# Original Probe

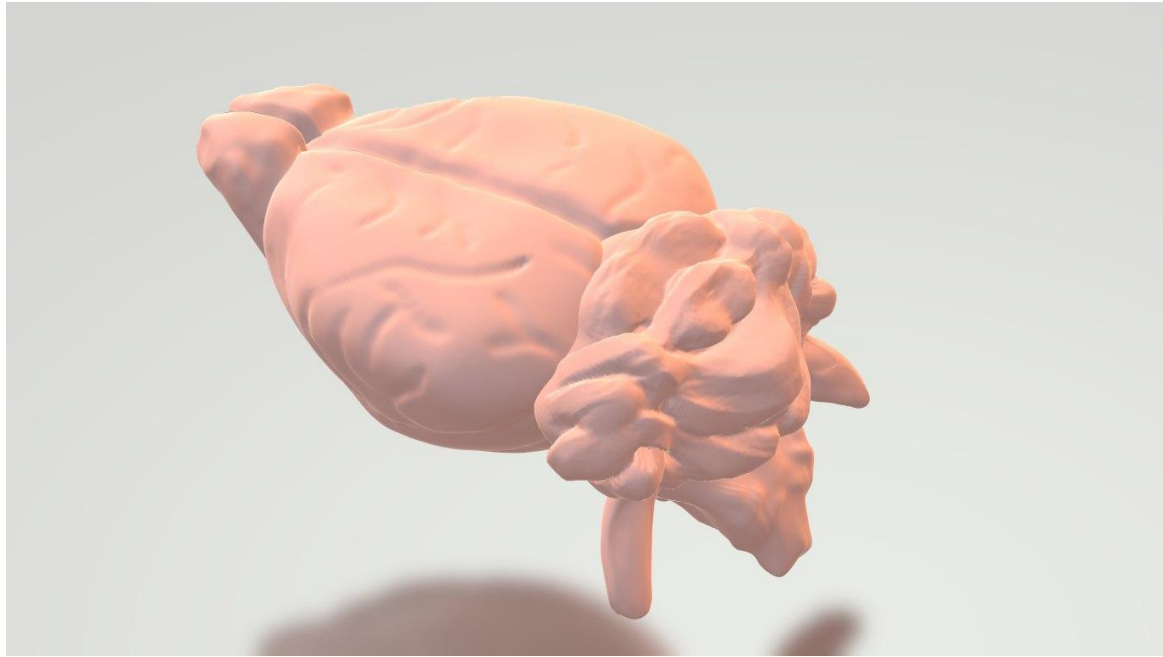
	Antibody 1	IgG antibody 1	Antibody 3	Antibody 4	IgG antibody 2	IgG antibody 3
Average Absorbance	.2545	.226	.219	.2435	.223	.222
Protein Concentration (mg/mL)	.179	.139	.129	.163	.135	.133
Percent Conjugation	35.74%	27.76%	25.80%	32.66%	26.92%	26.64%

# Modified Probe

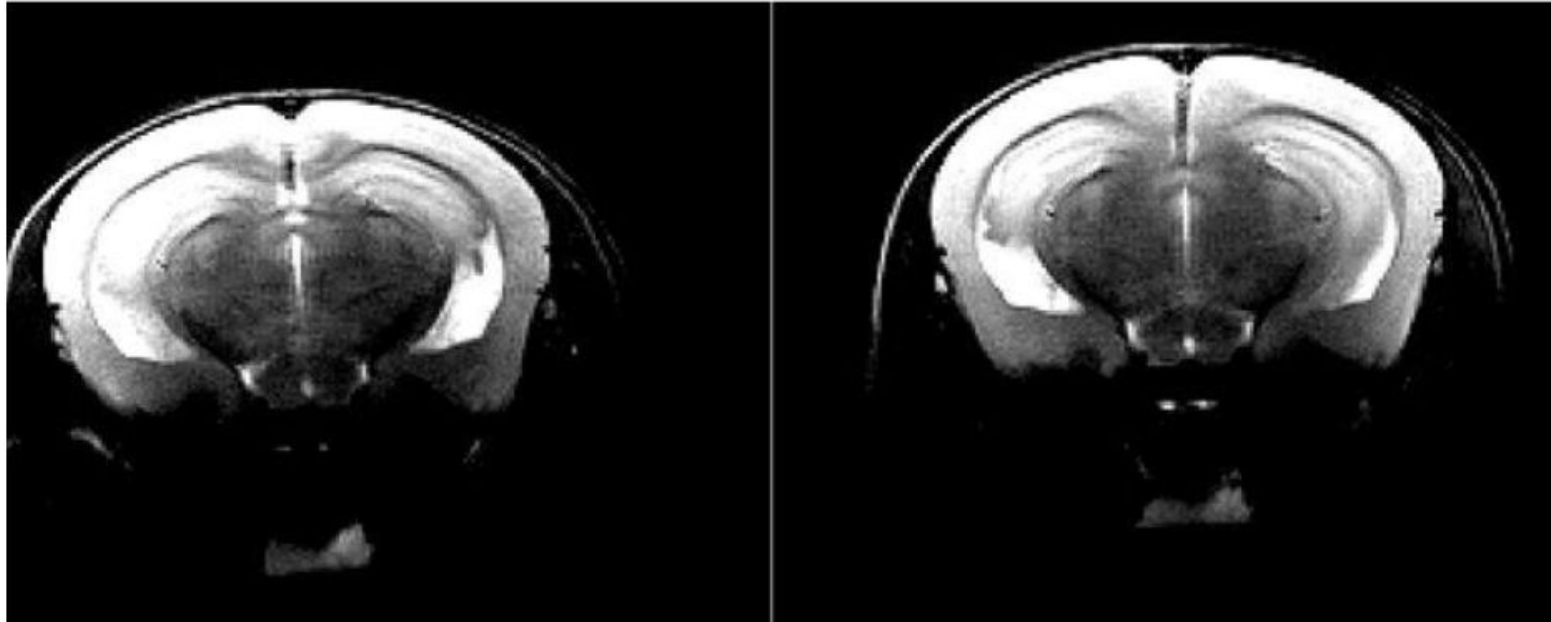
	Original ACU193 Sample	After 1 Conjugation Flow-Through	After 2 Conjugation Flow-Throughs
Average	0.109	0.1085	1.866
Protein Concentration (mg/mL)	-0.054	-0.054	2.134
Percent Conjugation	0%	0%	71.3%

# Mice Data

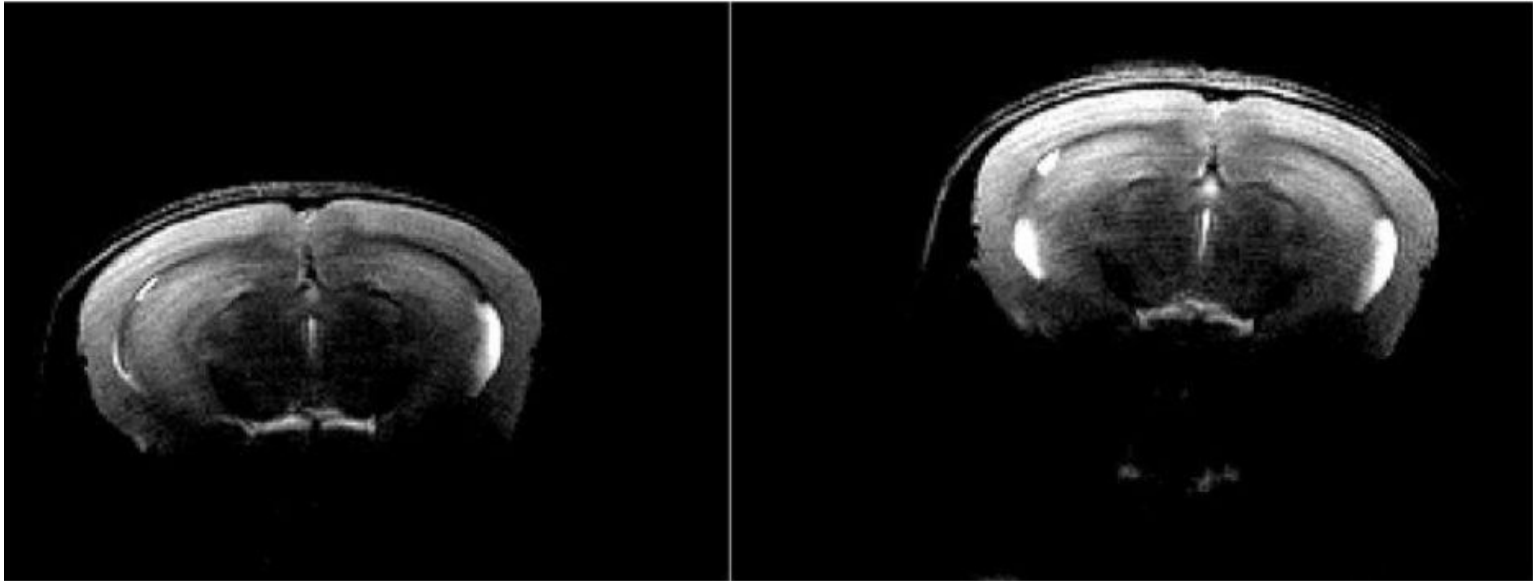
# Mouse Brain Model



# Wild Type Mouse with Probe



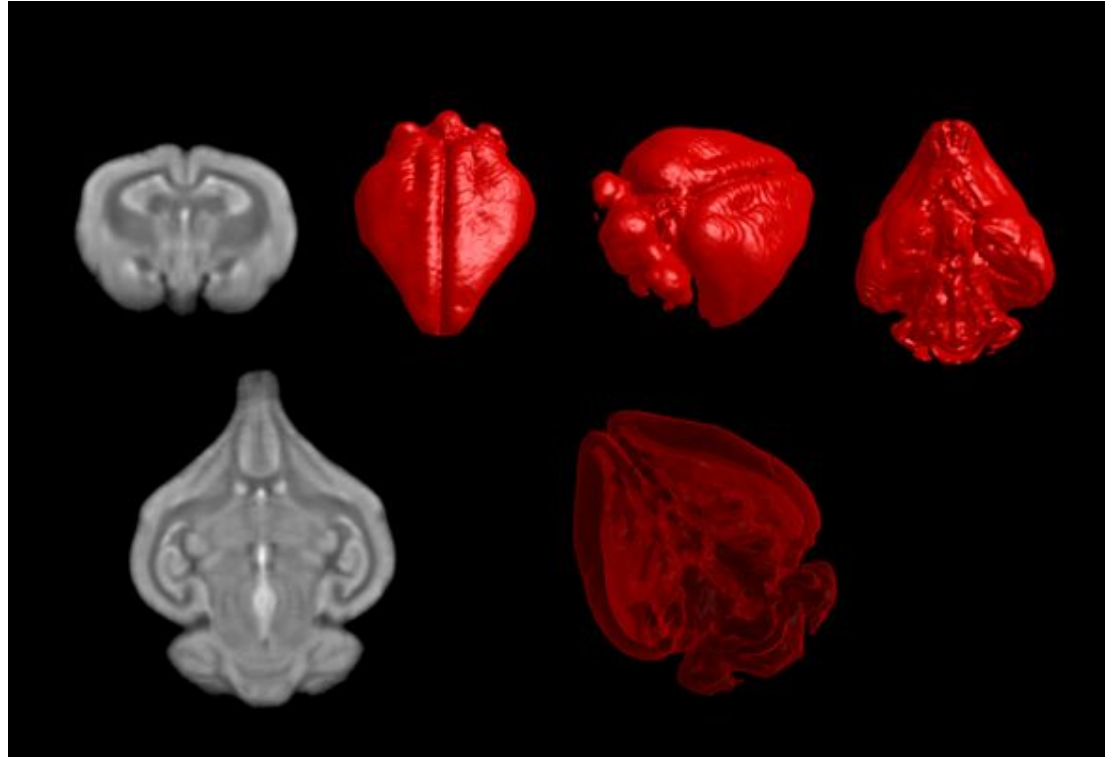
# Transgenic (5XFAD) Mouse with Probe



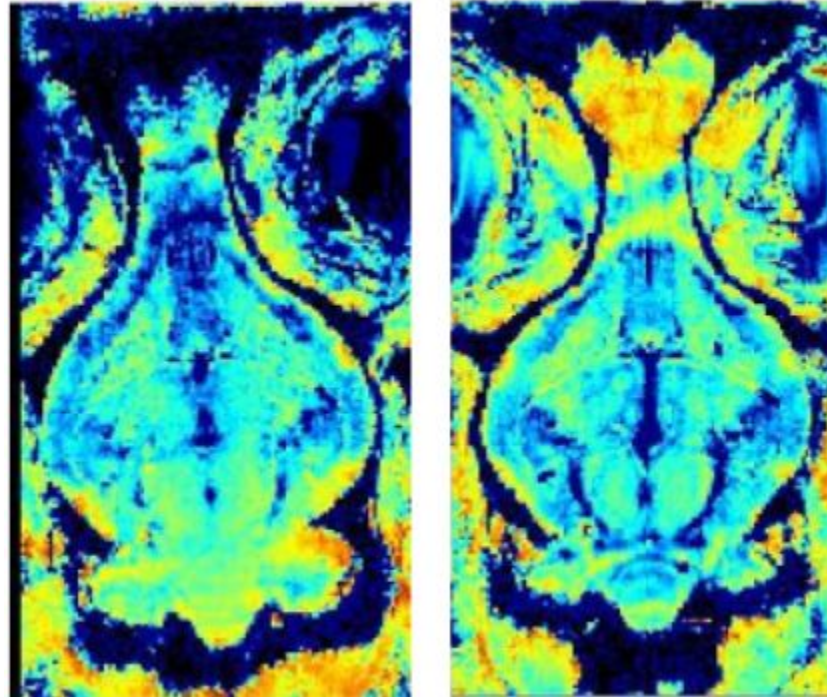
# Rabbit Data



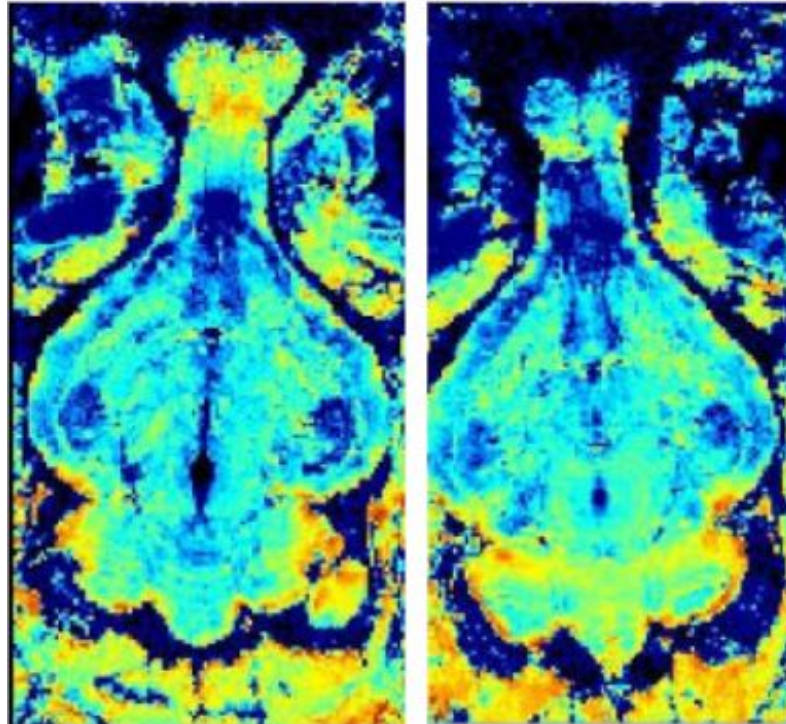
# Rabbit Brain Model



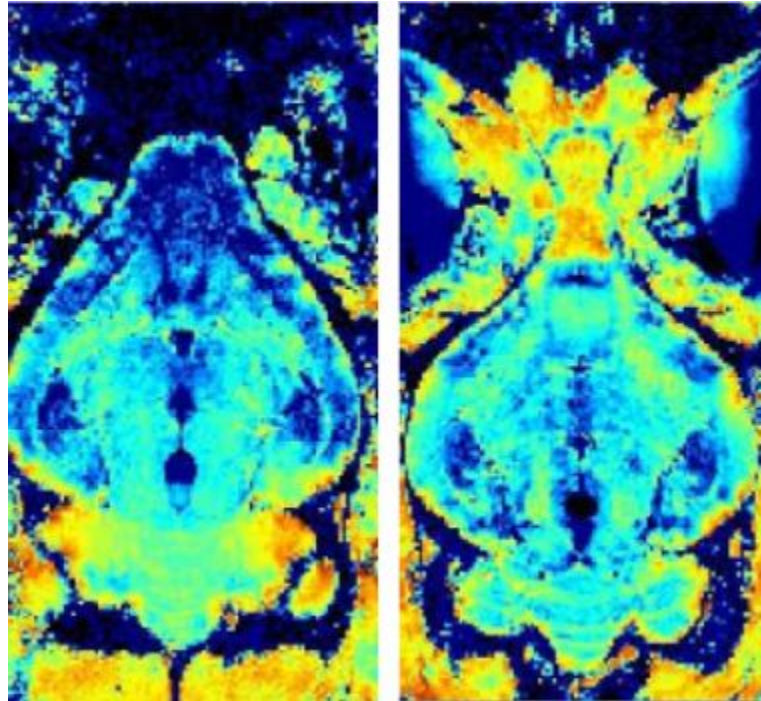
# High Cholesterol Diet Rabbit with Probe



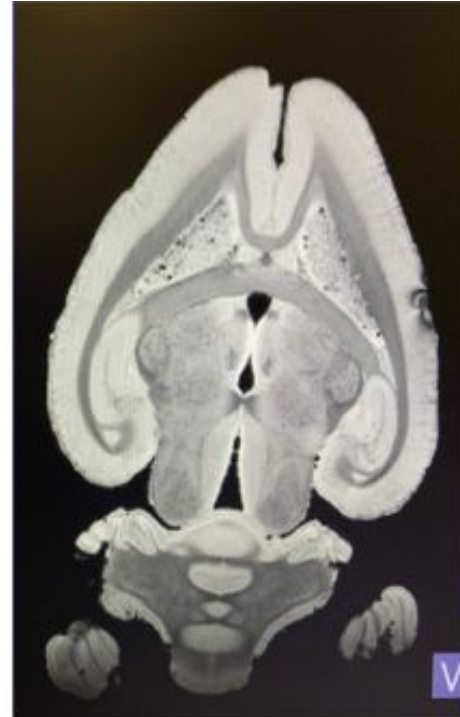
# High Fructose Diet Rabbit with Probe



# Control Diet Rabbit with Probe



# Rabbit Ex Vivo Imaging



# Conclusion and Future Research

- Double conjugation method of probe = higher percent conjugations
- Probe effective in mouse model
- Probe effective in preliminary rabbit model tests
- **Future Research:**
  - Achieve higher conjugation efficiency in probe
  - Continue testing probe in rabbit model
  - Eventually test probe in more complex animal
  - Create human-diagnostic methodology

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