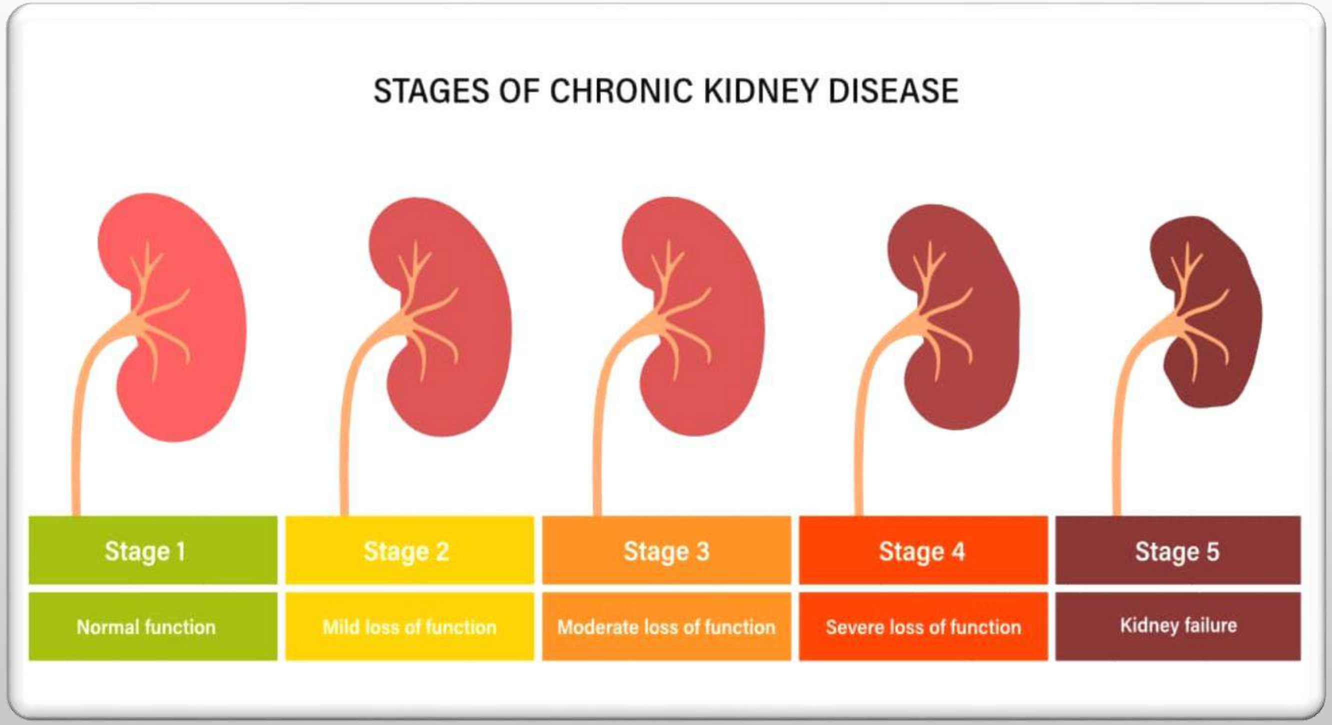
PRESENTED BY INDYYA HARVEY

TOWARDS EARLY DETECTION OF DIABETIC KIDNEY DISEASE USING CONTRAST ENHANCED ULTRASOUND PERFUSION PARAMETERS

DIABETES

- AFFECTS OVER 34.2 MILLION AMERICANS AS OF 2018 (~10%)
- RISK FACTOR FOR OTHER COMPLICATIONS (I.E CARDIOVASCULAR DISEASE)
- LEADING CAUSE OF CHRONIC KIDNEY DISEASES
- 40% OF PEOPLE WITH TYPE 2 DIABETES DEVELOP END STAGE KIDNEY DISEASE



WHY IT IS IMPORTANT TO DETECT DEVELOPING CKD BEFORE IT'S IDENTIFIED BY BLOOD AND URINE MARKERS

- Earlier detection could prevent further damage to the kidney
- Current markers Lags behind disease progression
- In need of earlier detection of disease progression
- Measuring Renal perfusion = faster feedback

CT Scans	MRI Scans	Ultrasound
• Uses Ionizing radiation • Increase risk of cancer • Expensive • Contrast agents do not stay confined to the blood vessel • Contrast agents not safe for compromised kidneys	• More expensive • Not well tolerated by some patients • Does not use ionizing radiation • Contrast agents do not stay confined to the blood vessel • Contrast agents not safe for compromised kidneys	• Inexpensive • Portable • Does not use ionizing radiation • Contrast agents are safe for use in compromised kidneys • Contrast agents are true blood markers

CT VS MRI VS UTRASOUND

Microbubbles

Contrast agents serve as a marker for kidney perfusion

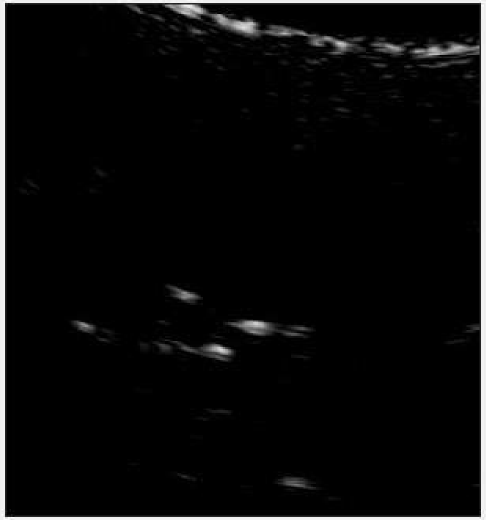
Act as a tracer for blood flow

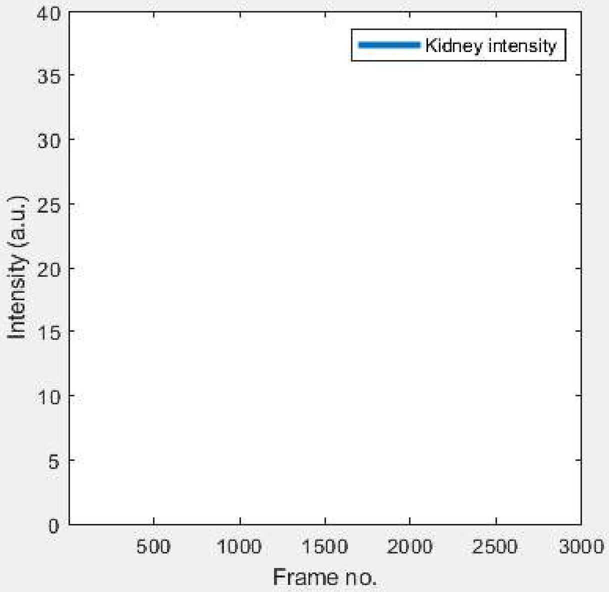
Small; gas filled particle with a lipid shell

Similar size and flow behavior as red blood cells

METHOD

- ONLY INTERESTED IN SIGNAL AND BLOOD FLOW IN THE KIDNEY
- MEASURE CHANGES IN MICROBUBBLE'S INTENSITY OVER TIME
- WASH IN/WASH OUT METHOD
  - INDICATOR DILUTION MODELS
  - EXTRACT PERFUSION METRICS





PERFUSION MODELS

Log-normal

- Vessel branching
- $\frac{AUC}{t\sigma\sqrt{2\pi}}e^{-\frac{(\ln(t)-\mu)^2}{2\sigma^2}}$

Lagged-normal

- Transit through a large vessel followed by dispersion to smaller vessels
- $\int_{-\infty}^{t} f(\tau)g(t-\tau)d\tau$
  - Alternative equation to Lagged normal
    - AUC$\frac{1}{2}K[1+\mathrm{erf}(L)]$
    - K=λe[-λt-$\frac{\mu^2}{2\sigma^2}+\frac{(\mu+\lambda\sigma^2)^2}{2\sigma^2}$]
    - L=$\frac{t-\mu-\lambda\sigma^2}{\sqrt{(2\sigma^2)}}$

Gamma variate

- Compartmental flow
- $c_0\,\frac{e^{-\frac{t}{\tau}}(\frac{t}{\tau})^{k-1}}{t\Gamma(k)}$

PARAMETERS WE ARE USING

MTT (Mean Transit Time)

Average time that it takes for the M.B to move through kidney

Log-normal $= e^{\mu+\sigma^2}$

Lagged-normal $= \mu + \frac{1}{\lambda}$

Gamma $= \tau k$

TP (Time Peak intensity)

Time for max amount of Microbubble in the kidney

Log-normal $= e^{\mu-\sigma^2}$

Lagged-normal = Does not exist; no time origin

Gamma $= \tau(k-1)$

AUC(Area under the Curve)

Relative expression of blood volume in the Kidney

How many bubbles enter and leaves

Which best fits the raw data?

METHOD

Root mean squared error

- Fits the Perfusion model to Raw data
- Looks at the distance between the raw data and the model
- How well does this model fit with the raw data?

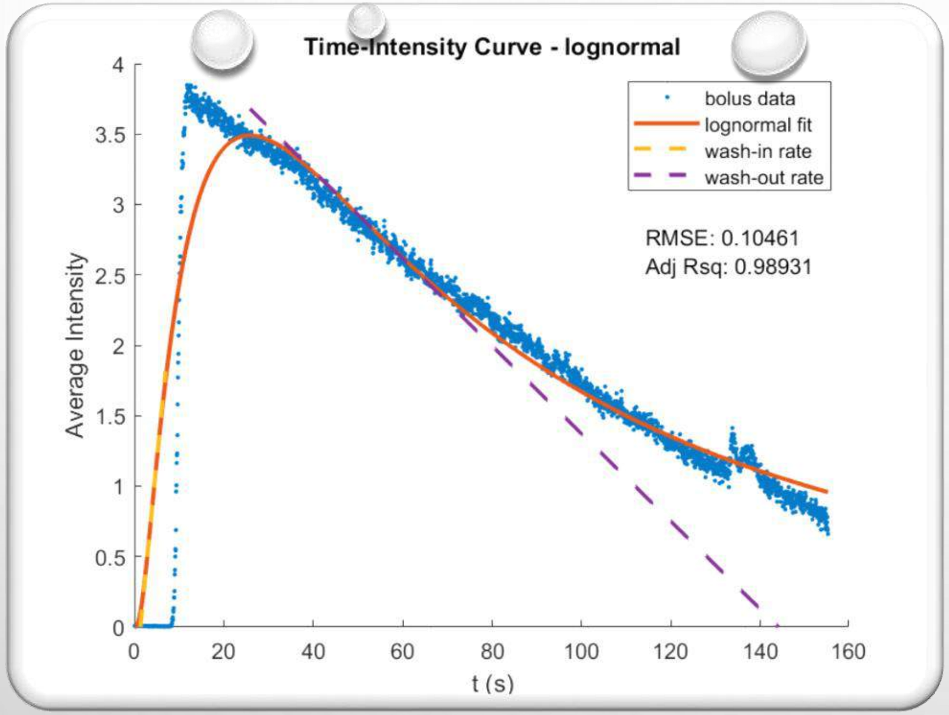
R^2

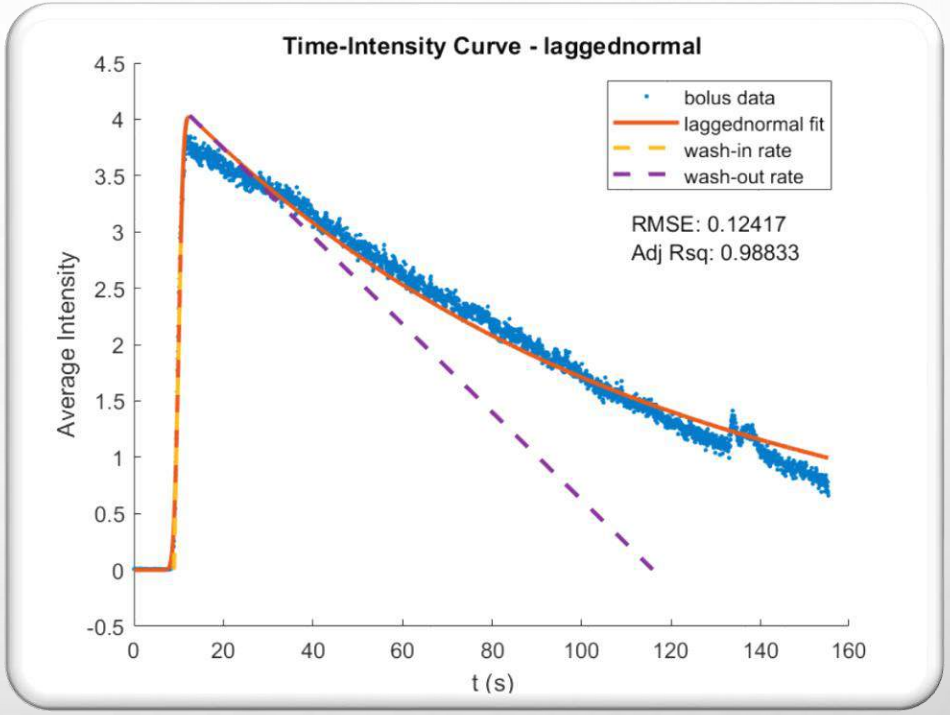
- Another method for looking at how well the model fits the raw data
- Value closer to 1 indicate a better fit between the model and data
- A value of 1 indicates a perfect fit

Goal

- Minimize RMSE
- Maximize R^2 value

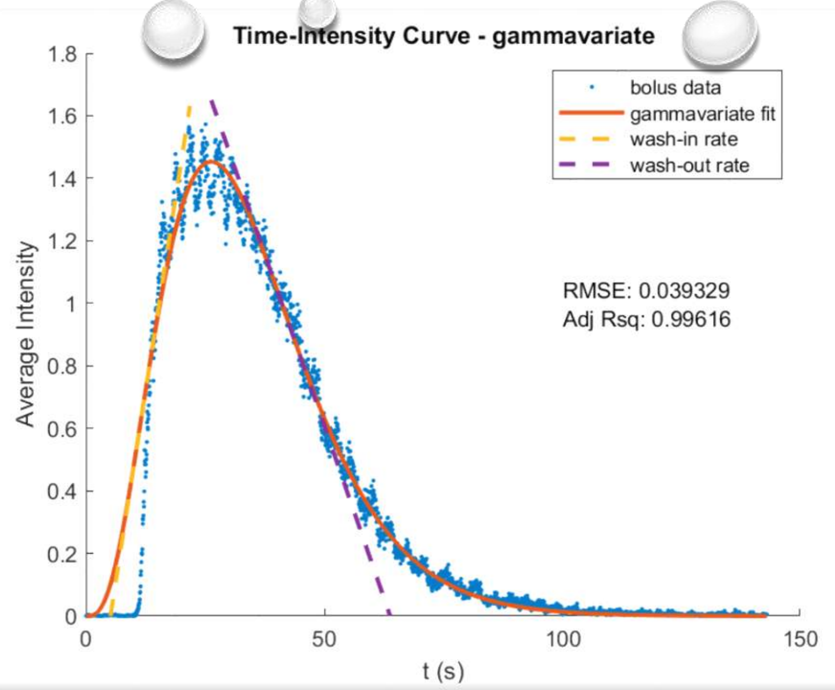
MODEL COMPARISON

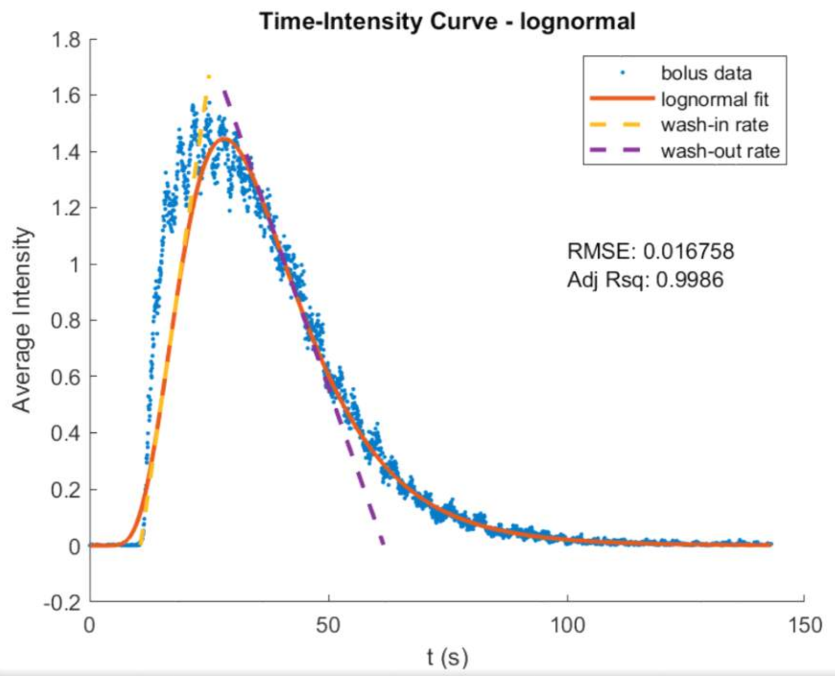




Model	PE	TP	MTT	RT	FT	WiR	WoR	WiAUC	WoAUC
Lagged	4.0	12.39	44.99	3.43	103.54	1.93	-0.039	9.67	262.34
Log	3.49	35.11	89.51	33.72	178.81	0.189	-0.015	64.61	282.63

MODEL COMPARISON





Model	PE	TP	MTT	RT	FT	WiR	WoR	WiAUC	WoAUC
Gamma	1.45	26.28	26.77	21.14	37.53	0.0979	-0.043	19.52	31.92
Log	1.44	28.17	23.16	17.51	33.43	0.116	-0.048	15.99	28.39

DISCUSSION

- THERE IS A CLEAR DIFFERENCE BETWEEN LAGGED AND LOG NORMAL
- GAMMA VARIATE AND LOG NORMAL ARE MUCH MORE SIMILAR MODELS
- FOR THE DIABETIC EXAMPLE,
    - TAKES A LONGER TIME TO WASH OUT
    - PE IS HIGHER, POSSIBLY LARGER BLOOD VOLUME
    - MTT IS LONGER
- FOR THE CONTROL EXAMPLE,
    - WOAUC IS SMALLER
    - FALL TIME IS QUICKER
    - MTT IS FASTER
- APPLY THESE MODELS TO A MUCH LARGER SAMPLE SIZE
- **QUESTION**:
    - SHOULD WE FOCUS MORE ON RMSE OR FITTING THE DATA TO THE PARAMETERS?