KRANOS: K40 Radiations for Advanced Neuroimaging of Stroke

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12th June 2023

DESY Zeuthen Particle Physics Mini-Retreat

Stroke

- A neurological disorder , sudden loss of brain function
- Permanent brain tissue damage
- 12.2 million strokes per year (one every 3 seconds)
- Leading cause of death and disability
- Estimated global burden 451 billion $.

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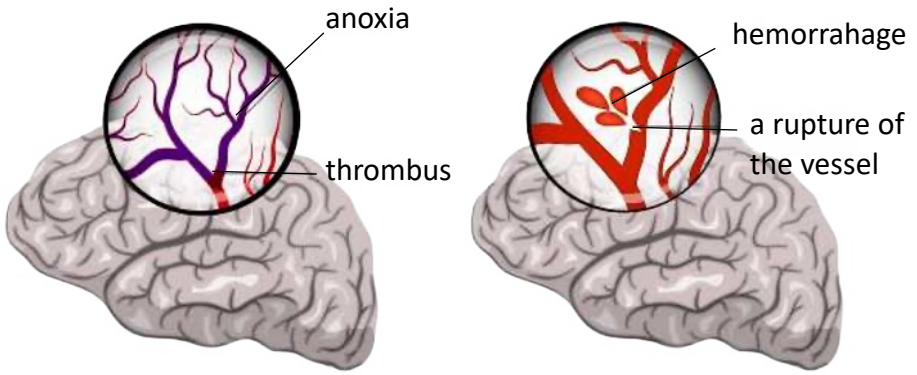
Types of Stroke



Ischemic stroke: Blockage of blood flow to the brain due to a clot.

Hemorrhagic stroke: Bleeding in or around the brain from a ruptured blood vessel.

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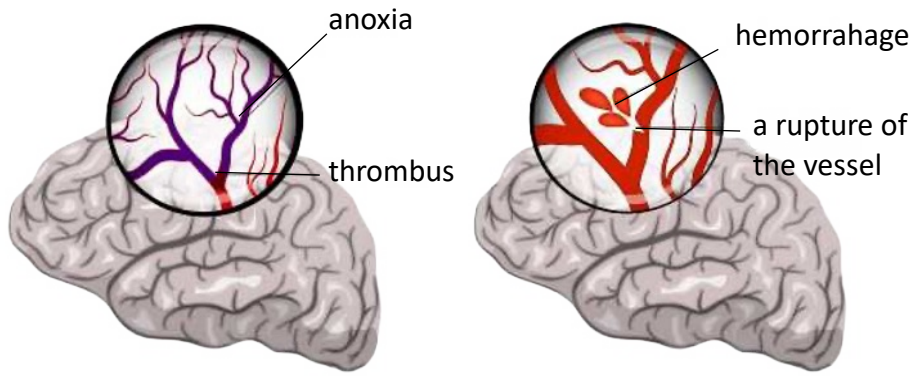

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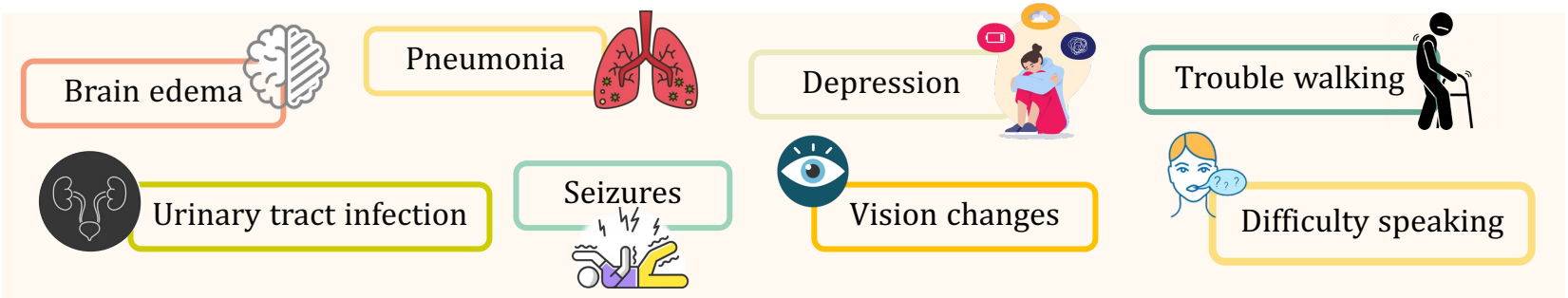
Stroke Complications and Implications



Current Diagnostic Methods and their Limitations

Limited time window for accurate diagnosis

Often starts after stroke symptoms appear

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True positive 82%, True negative 83%

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Computed Tomography (CT)

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True positive 58%, True negative 85%

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Sees tissues not elements

High Cost (~0.5 M)

Not Portable (typical)

Trained professionals

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High Cost (~0.5 M)

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Trained professionals

Magnetic Resonance Image (MRI)

3

True positive 80-90%,

True negative 97%

Long acquisition time

High Cost (>1M Euro)

Not Portable, heavy

Specialized professionals

Potassium and Stroke Correlation

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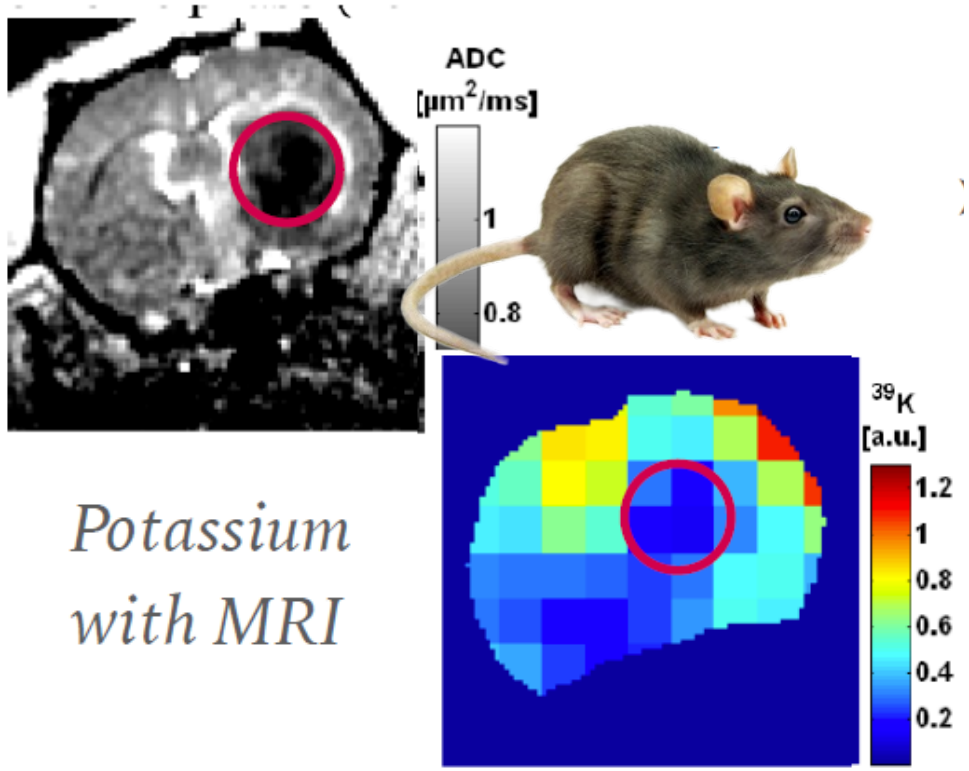

Potassium with MRI

[1] Proc. Intl. Soc. Mag. Reson. Med. 20 (2012)

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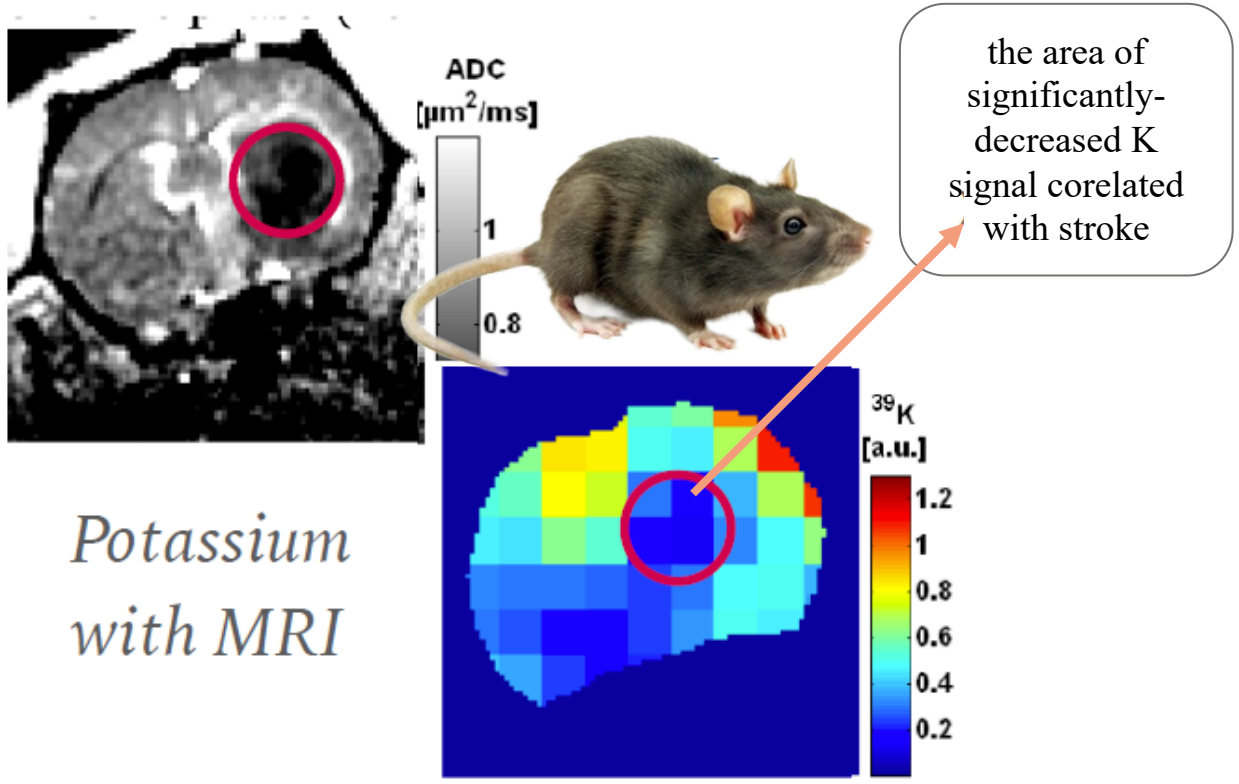

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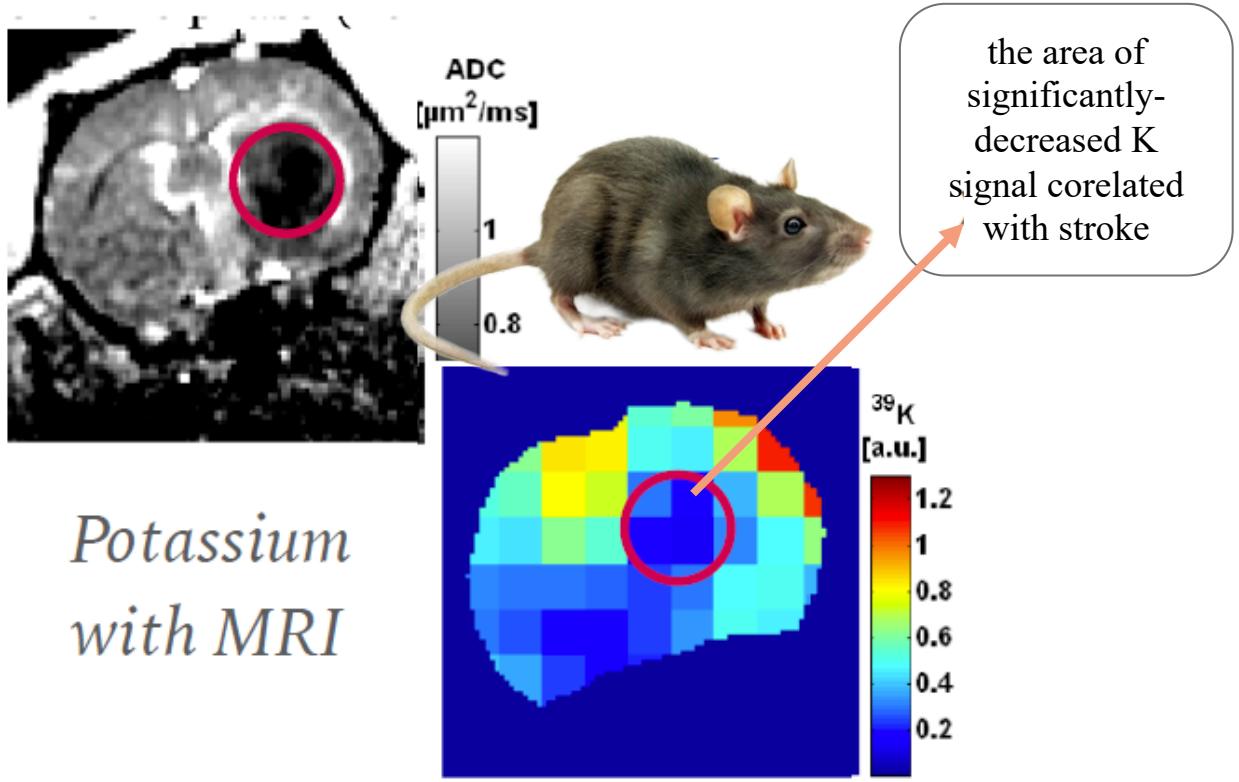

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MRI Rat brain study showed that potassium distribution in the brain can be used as a biomarker for strokes

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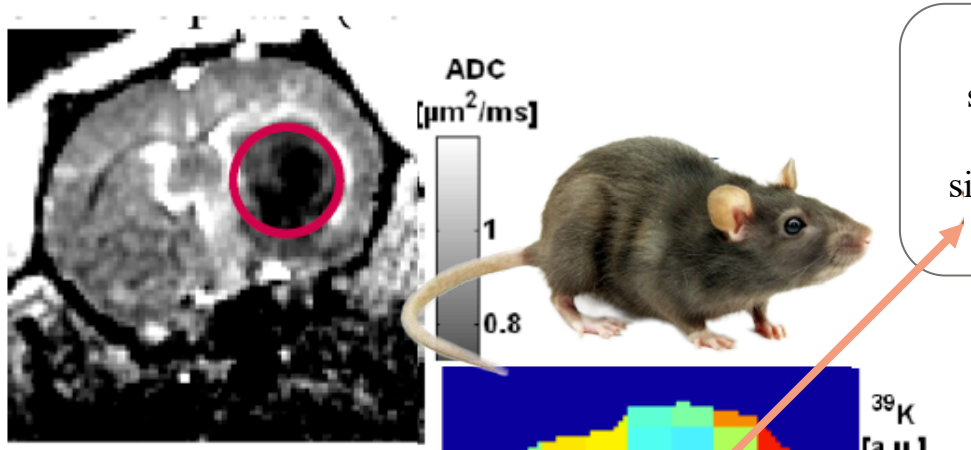

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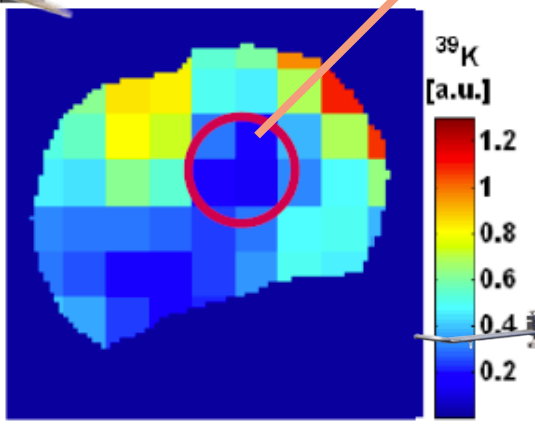

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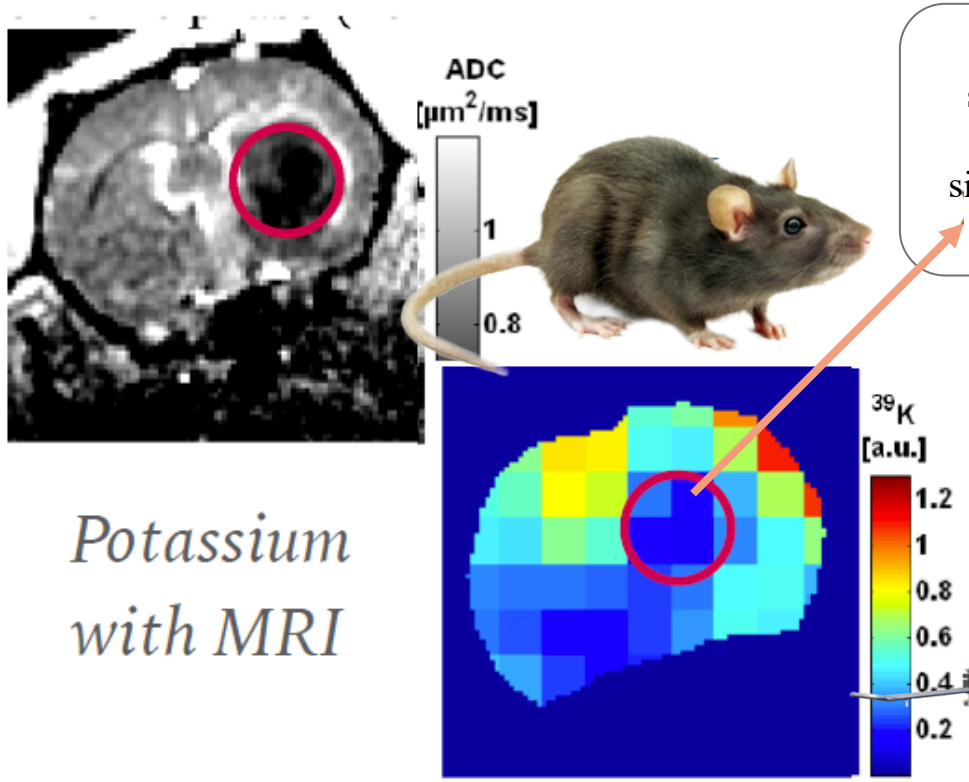

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Naturally Occurring Isotopes of Potassium

Isotope Notation	Natural Abundance (%)	Atomic Mass	State
K-39	93	38.96	stable
K-40	0.01	39.96	1.28 × 10^9 years
K-41	6.7	40.96	stable

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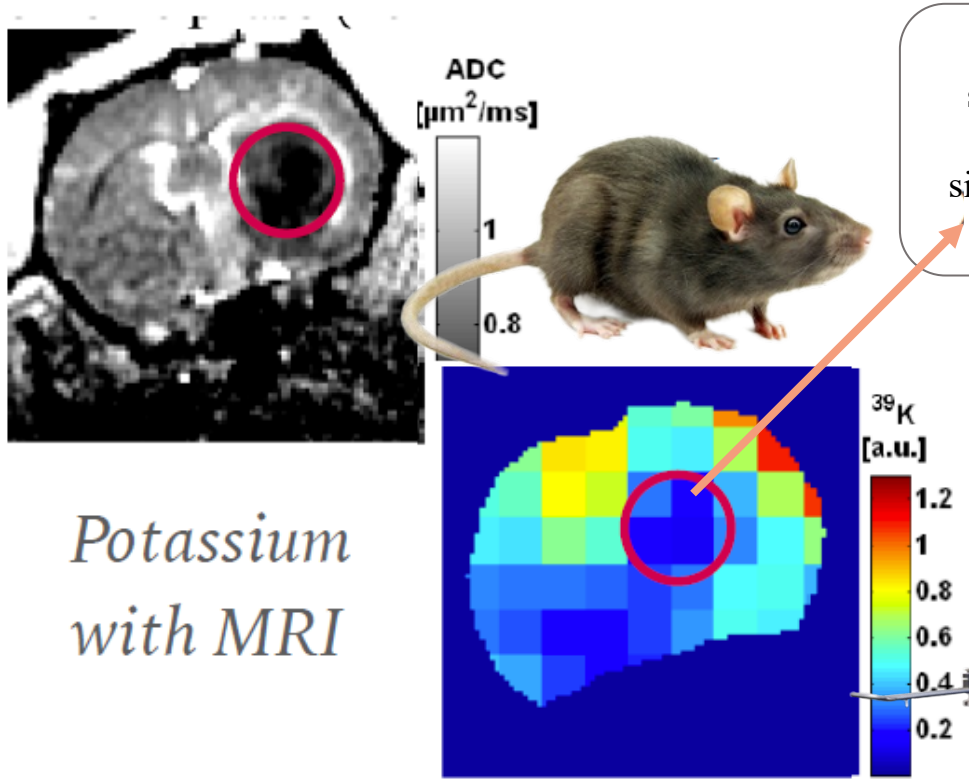

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KRANOS: Non invasive imaging of Potassium in the brain but instead of K39 will use the naturally radioactive K40 1.46MeV photons

The "natural" solution

Advantages, Objectives and Challenges of KRANOS

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1. Advantages

- ✓ **Quick diagnostic** – within window of recovery
- ✓ **Inexpensive** (Low income Countries)
- ✓ **Portable**
- ✓ **Radiation free**
- ✓ **Future** – population at risk
  Screeing
  personalised medicine

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2. Objectives

- ➢ Timely intervention during asphyxia to minimize the loss of brain cells
- ➢ High detection efficiency (= speed)
- ➢ Portability (= compact dimensions)
- ➢ Background rejection

Advantages, Objectives and Challenges of KRANOS

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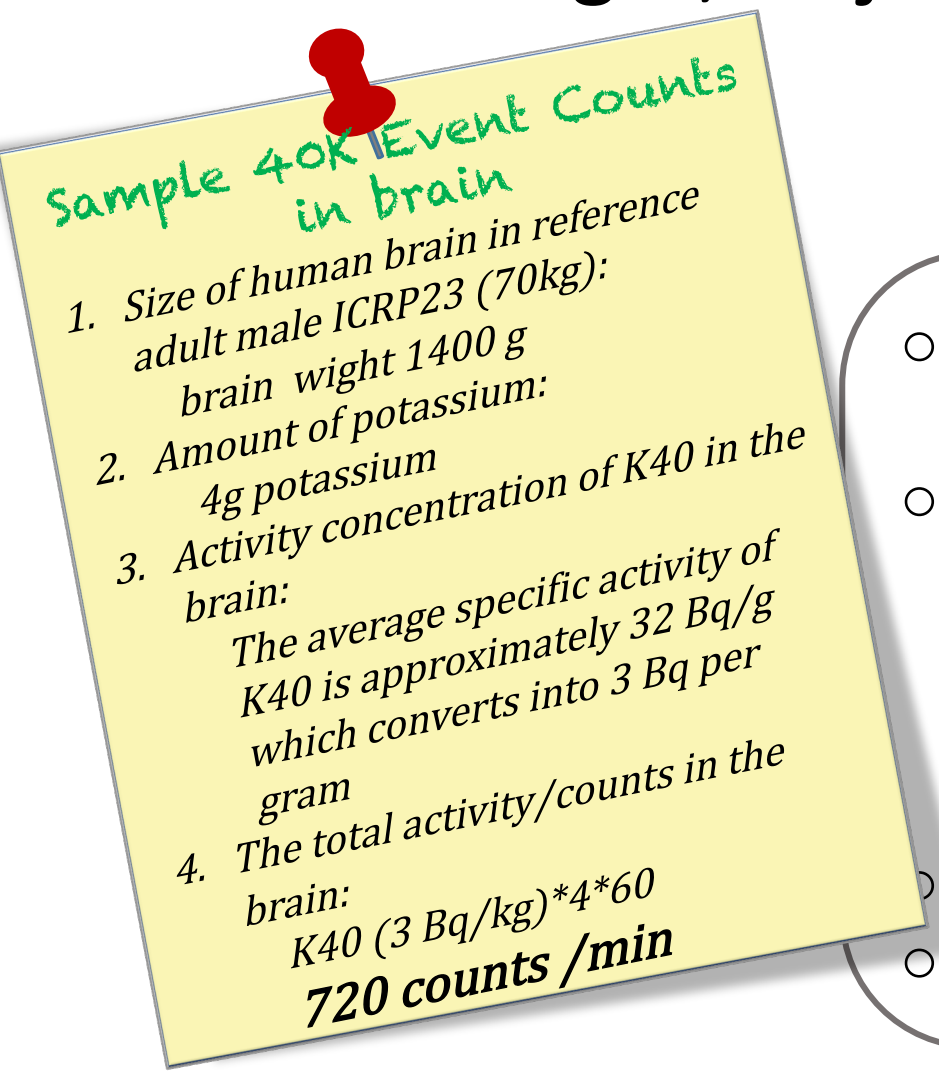
Sample 40K Event Counts in brain

1. Size of human brain in reference adult male ICRP23 (70kg):
   brain wight 1400 g
2. Amount of potassium:
   4g potassium
3. Activity concentration of K40 in the brain:
   The average specific activity of K40 is approximately 32 Bq/g which converts into 3 Bq per gram
4. The total activity/counts in the brain:
   K40 (3 Bq/kg)*4*60
   720 counts /min

3.Challenges

- K40 potassium in the human body is very low.
- Factors impacting counts
  - High sensitivity & Efficiency
  - Interaction probablity
  - Background radiation
- Speed?
- Price?

Advantages, Objectives and Challenges of KRANOS



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4.Tech Choices

- ❑ Scintillation Crystal: Chosen as primary detection material
- ❑ Idea ?? Maybe Compton Camera Technology in Later Stages

Technology Selection: Navigating the Choices

Considered Factors

- Sensitivity
- Acquision time
- Background radiations
- Price

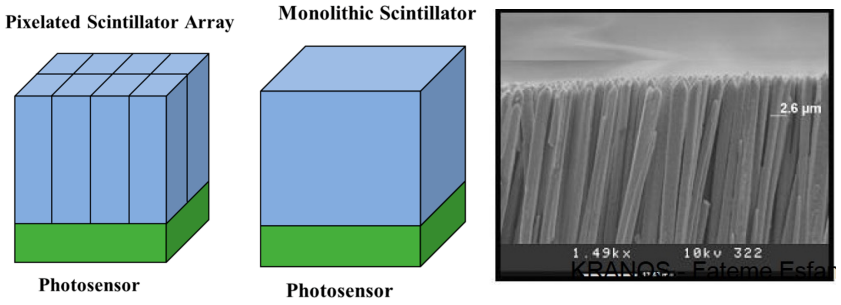
#	Detectors	# PE events	Energy Resolution (E=1.46MeV)	(PE events) *(Light Yield) (photons / MeV)	Price
1	NaI	12	7-8%	456,000	low
2	BGO	87	8.5%	783,000	high
3	LYSO	56	8.2%	1,848,000	high
4	GYGAG	18	3-5%	828,000	high
5	CeBr3	14	3.0%	840,000	Very high
			Competitive Semiconductors		
6	CdZnTe	16	1.5%		
7	CdTe	19	5.5%		

PE = Photoelectric events

Design Parameters

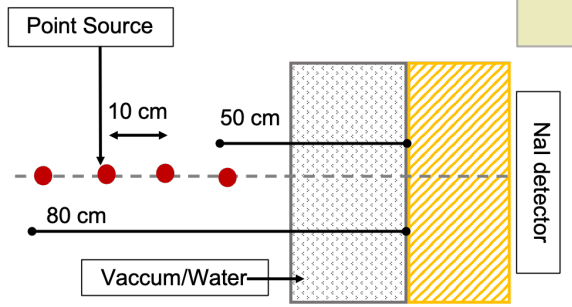
- Material composition
- Material Form
- System's Total structure

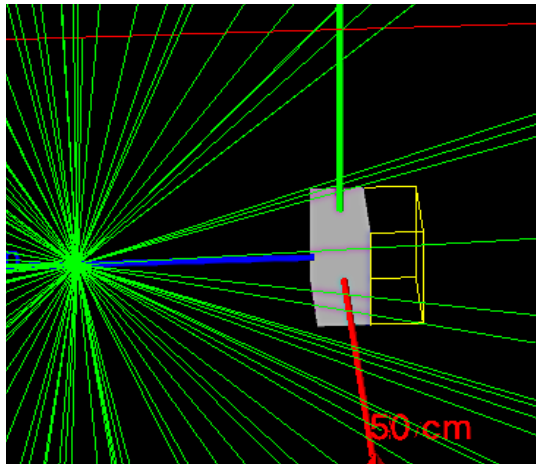
Detectors	Readout	Material Form
Scintillator	SiPM	1. Monolithic 2. Microcolumnar array (CsI) 3. Pixeleted (Array)

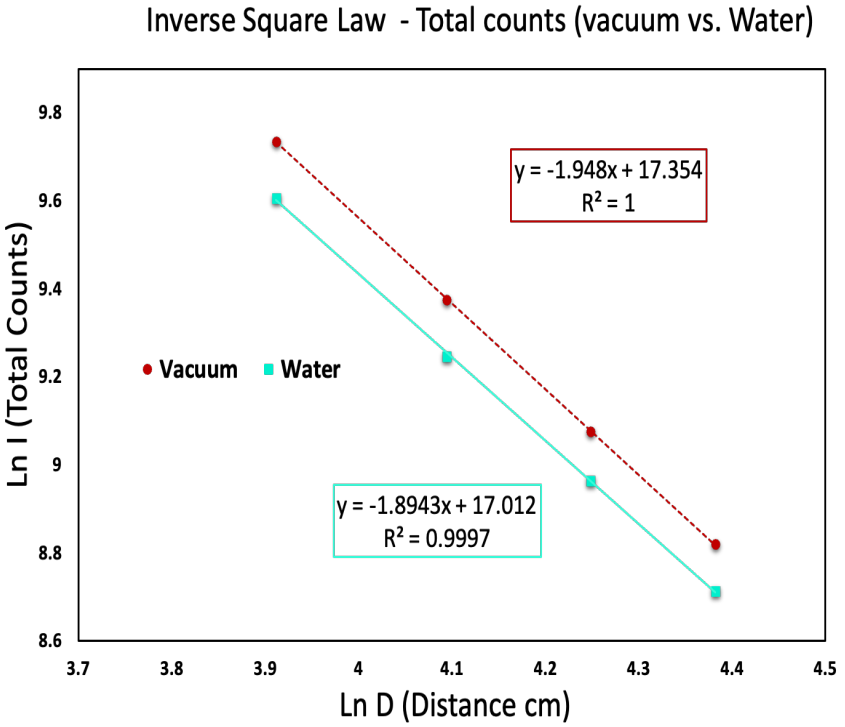


Simulations and Validation Studies

Validating gamma source







- Increased the distance of the point source from the detector
- Variation in observed counts fall as Inverse square of the distance

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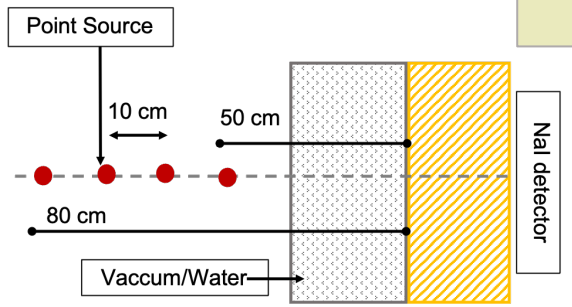
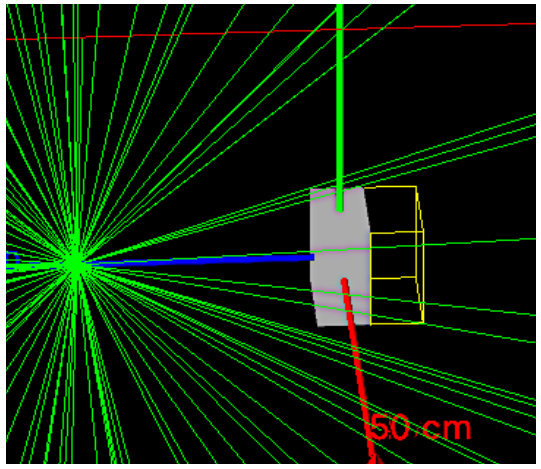
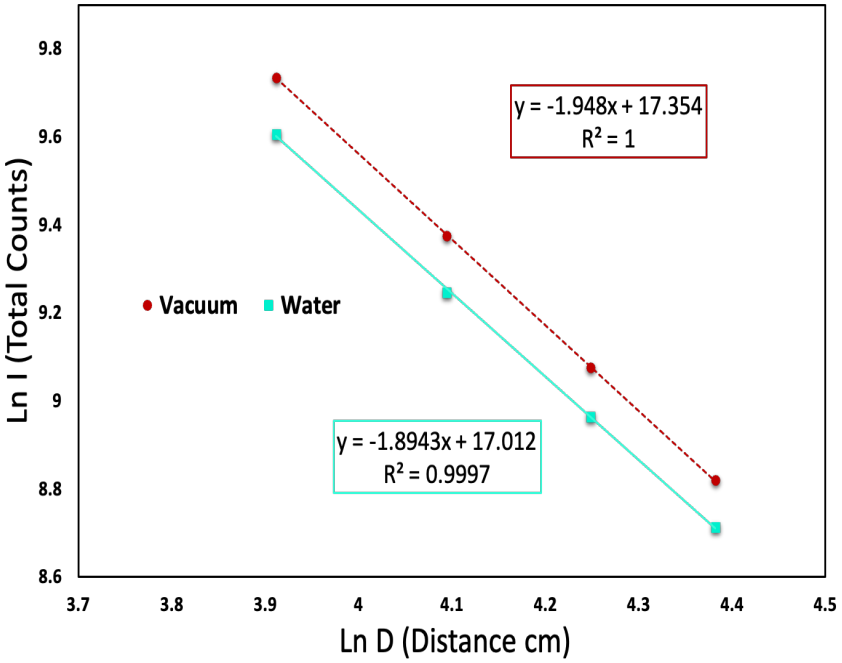




Inverse Square Law - Total counts (vacuum vs. Water)



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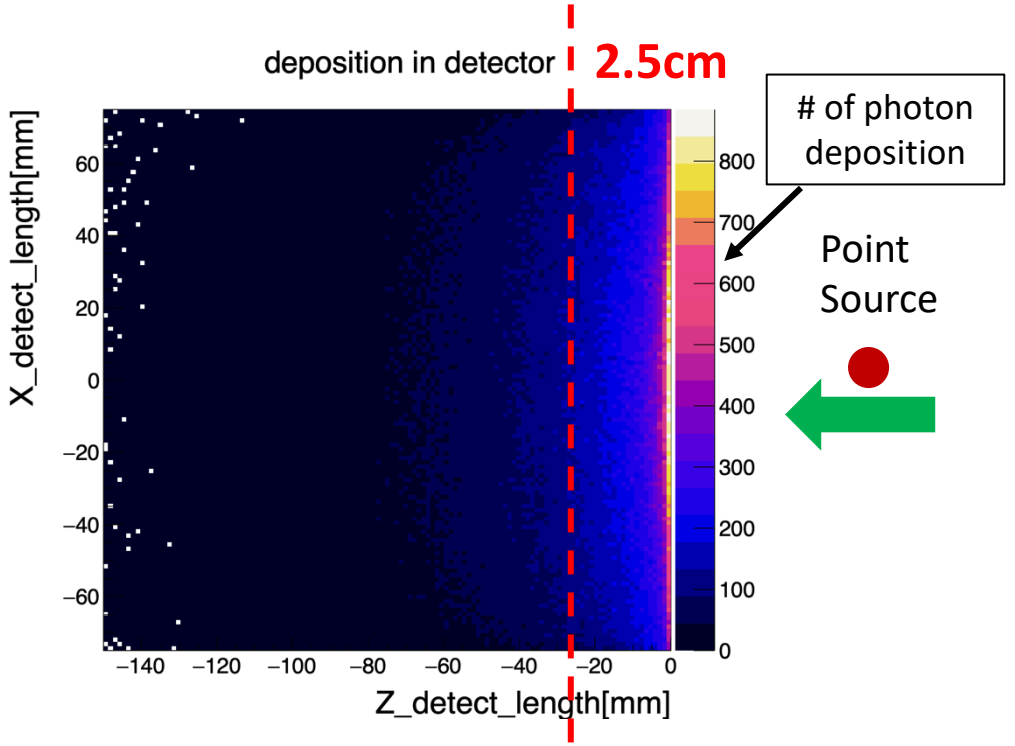
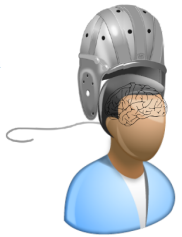
Scintillation Crystal Geometry



Conclusions:

Optimal thickness of detector was found to be 2.5cm with >95% absorptions of gamma

KRANOS Pathways



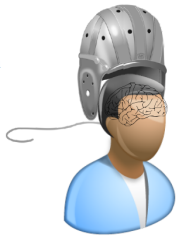
KRANOS Pathways

Optimization of design → Development of reconstruction algorithms → Development of background management algorithms → Proof of Principles (Lab Setup)

Secured funding:
- Desy Generator Program (1 postdoc)
- GoBio Initial (100K)

Close collaboration with Technology Transfer group to secure further fundings

Pending Applications:
- Tschira Boost Fund (80K - lab setup)
- Add-On Hertz Fellowship (12K – interdiscip-training)
- ILB Brandenburg Funding (50K - lab infrastructure)



Support Needed for Lab Establishment and Validation

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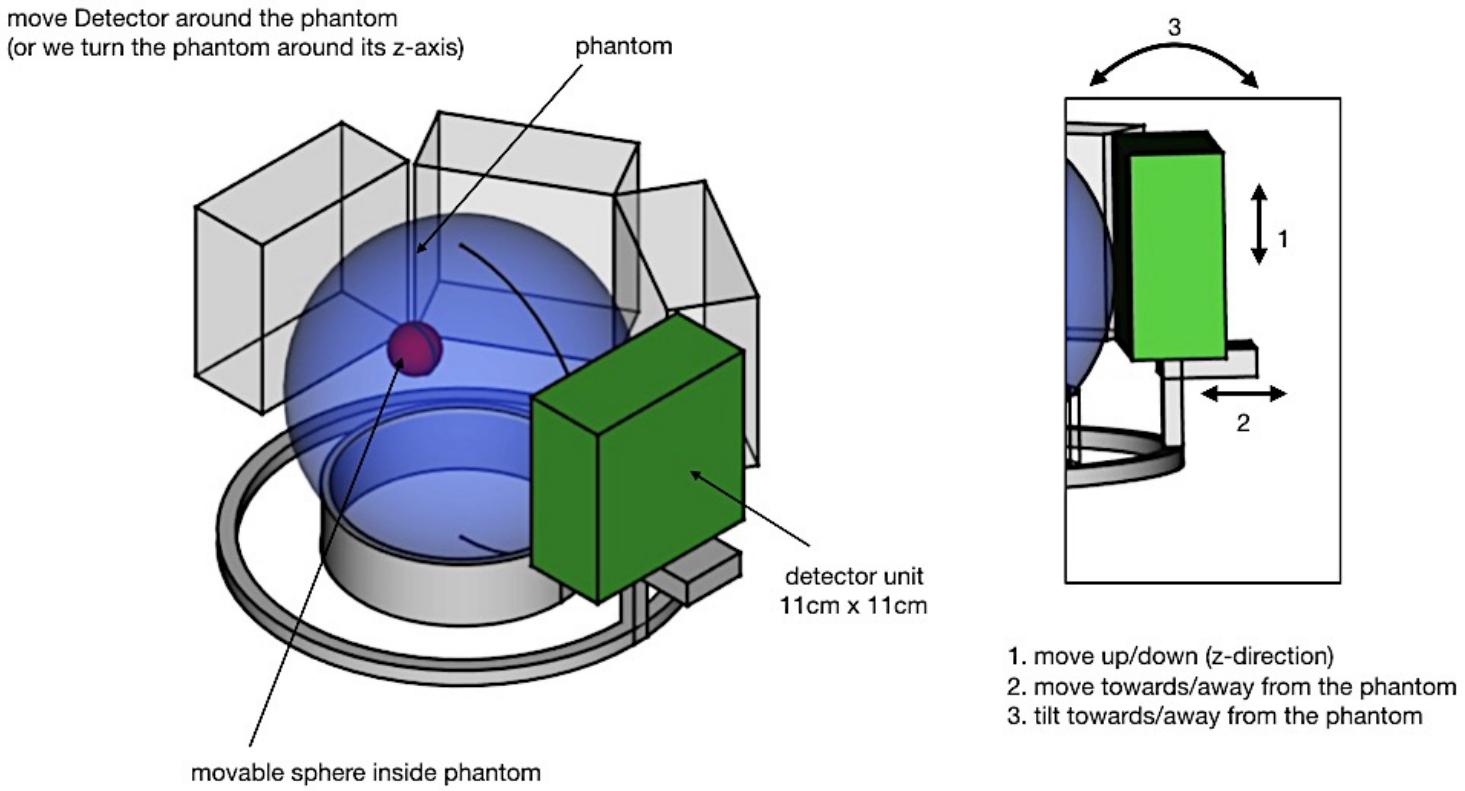
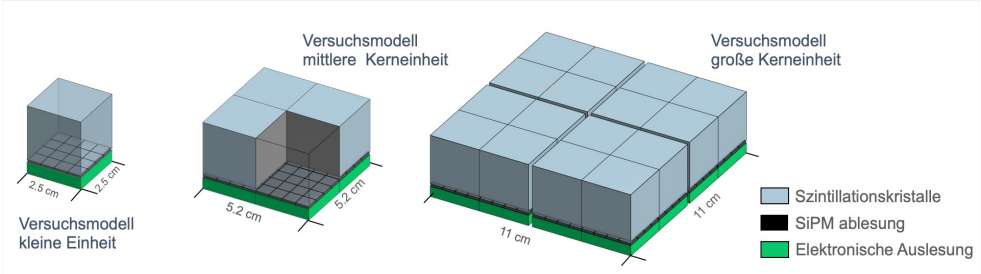
- Additional funding required for lab setup and system validation
- To conduct tests and to validate the functionality and performance of the imaging system
- Potential impact of our research in advancing brain imaging technology

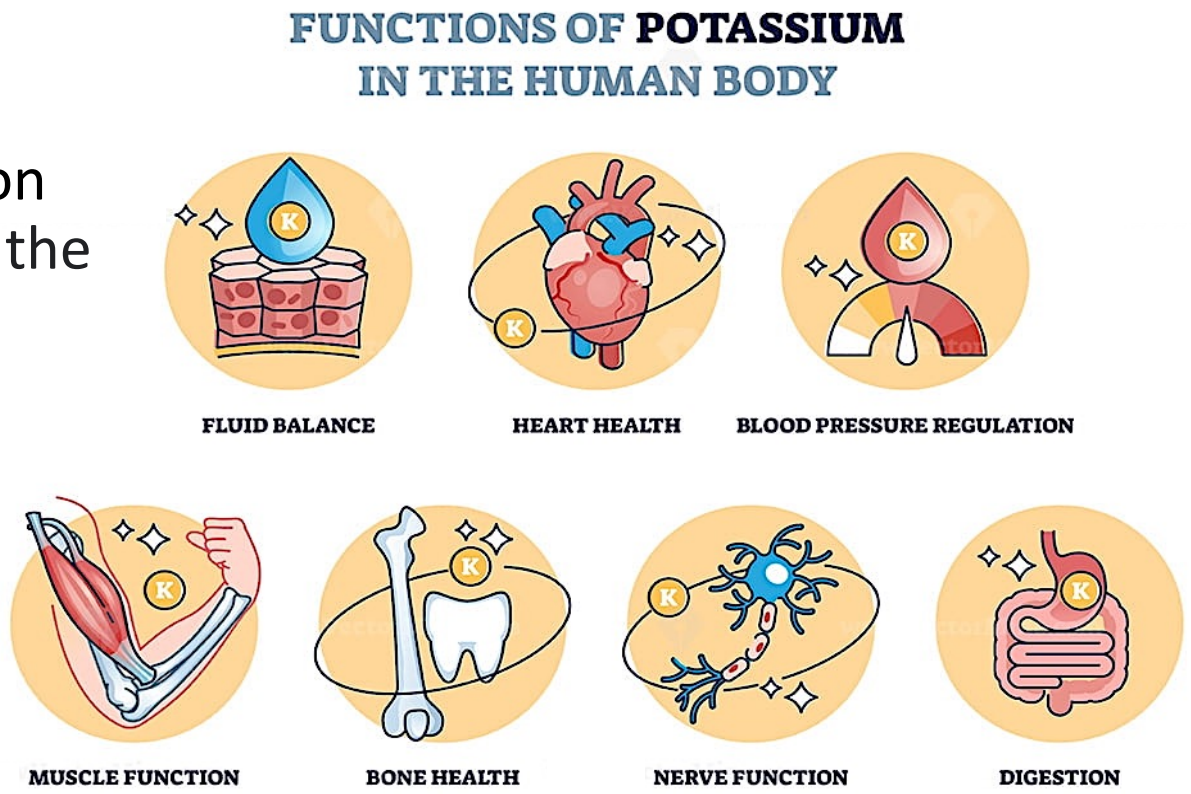


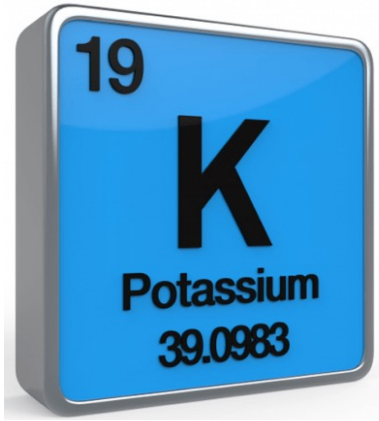


Thank You

Backup

Potassium is the most abundant intracellular ion and essential mineral in the human body





Vital element physiological functions : ➤Fluid balance ➤ Muscle contraction ➤Heart function ➤ Regulation of blood pressure ➤ nerve function

- Potassium homeostasis is crucial , excessive and insufficient levels
- **KRANOS**: Non invasive imaging of Potassium in the brain

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- Sudden loss of brain function and permanent brain tissue damage
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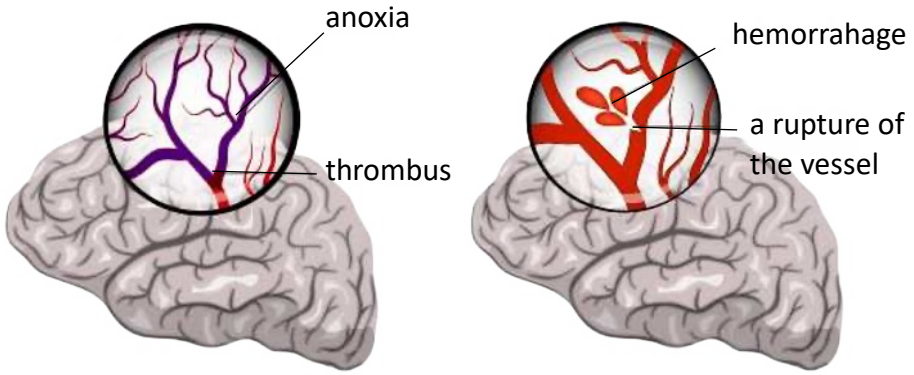
- Estimated global burden 451 billion $.



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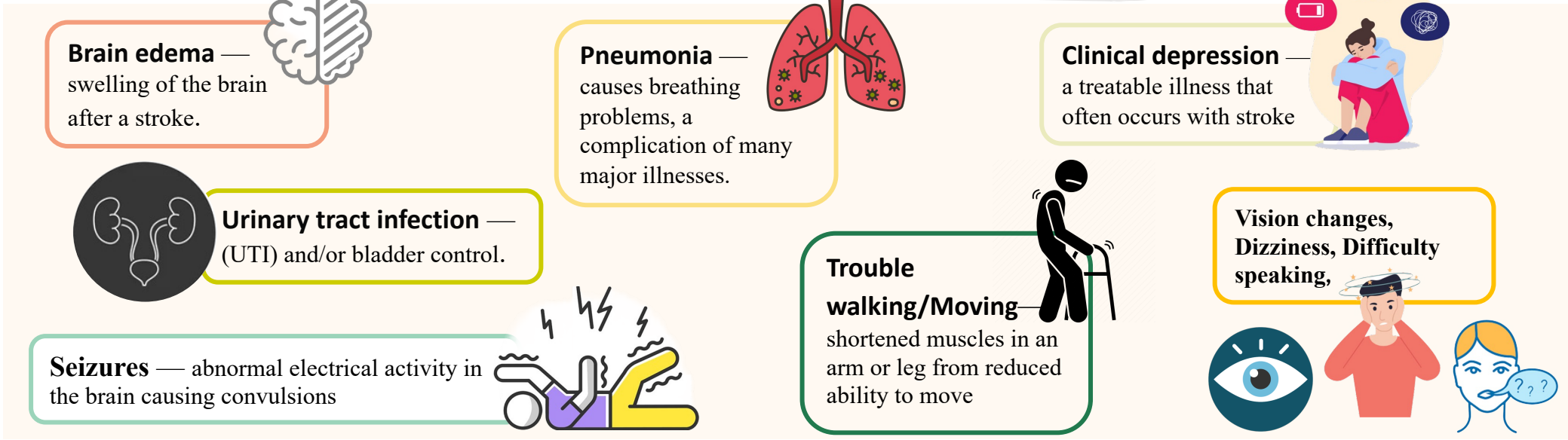

Potassium decay scheme

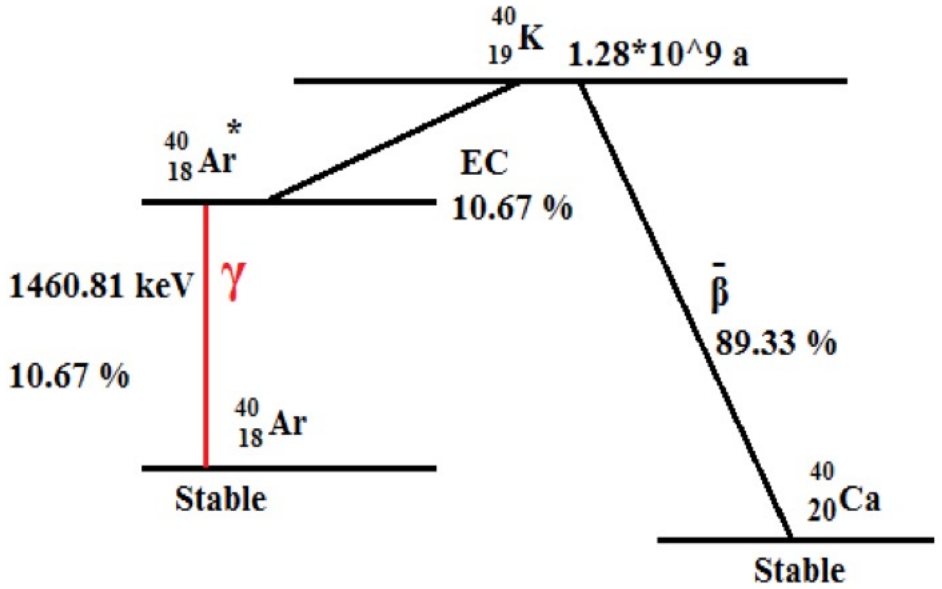

Fig.1.1 ^{40}K decay scheme

Impaired Energy Metabolism

- Impaired energy metabolism is a key pathological hallmark of ischemic stroke.
- A reduction in glucose and oxygen supply results in severe loss of ATP production in an ischemic brain.
- Cerebral ischemia disrupts mitochondrial oxidative metabolism and enhances mitochondria-mediated oxidative stress.