Using control charts to detect anomalous morphological measurements in brain imaging

Presenter: Sumner Williams

GOALS

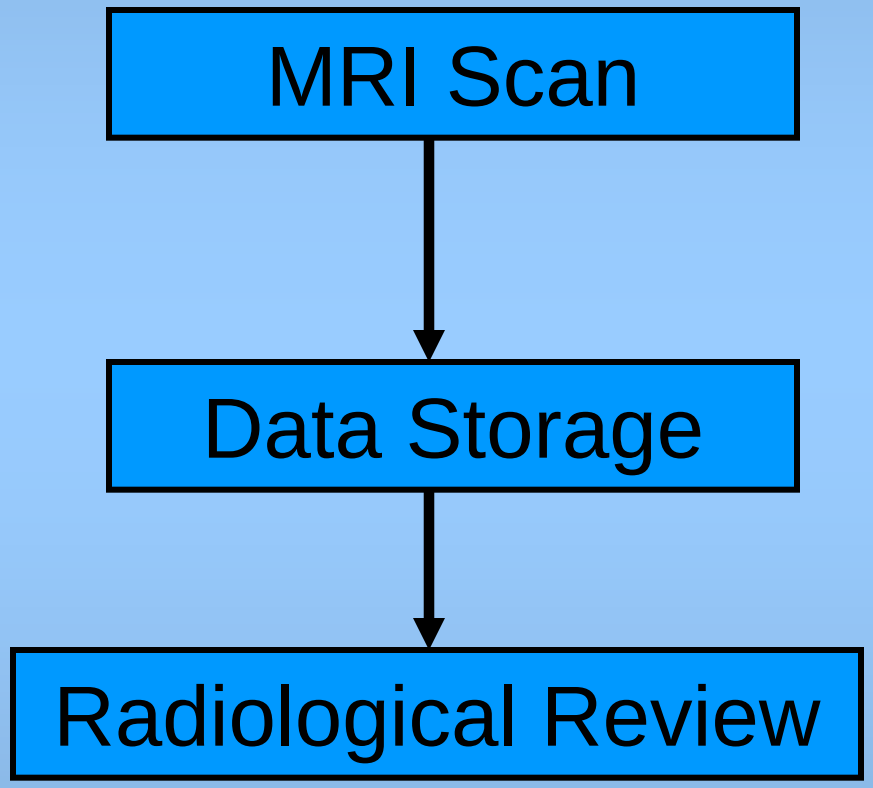
- Begin looking at using process control to detect aberrant brain volumes

- Decrease time it takes for a bad scan to be reviewed (currently about one week if too many scans were collected)

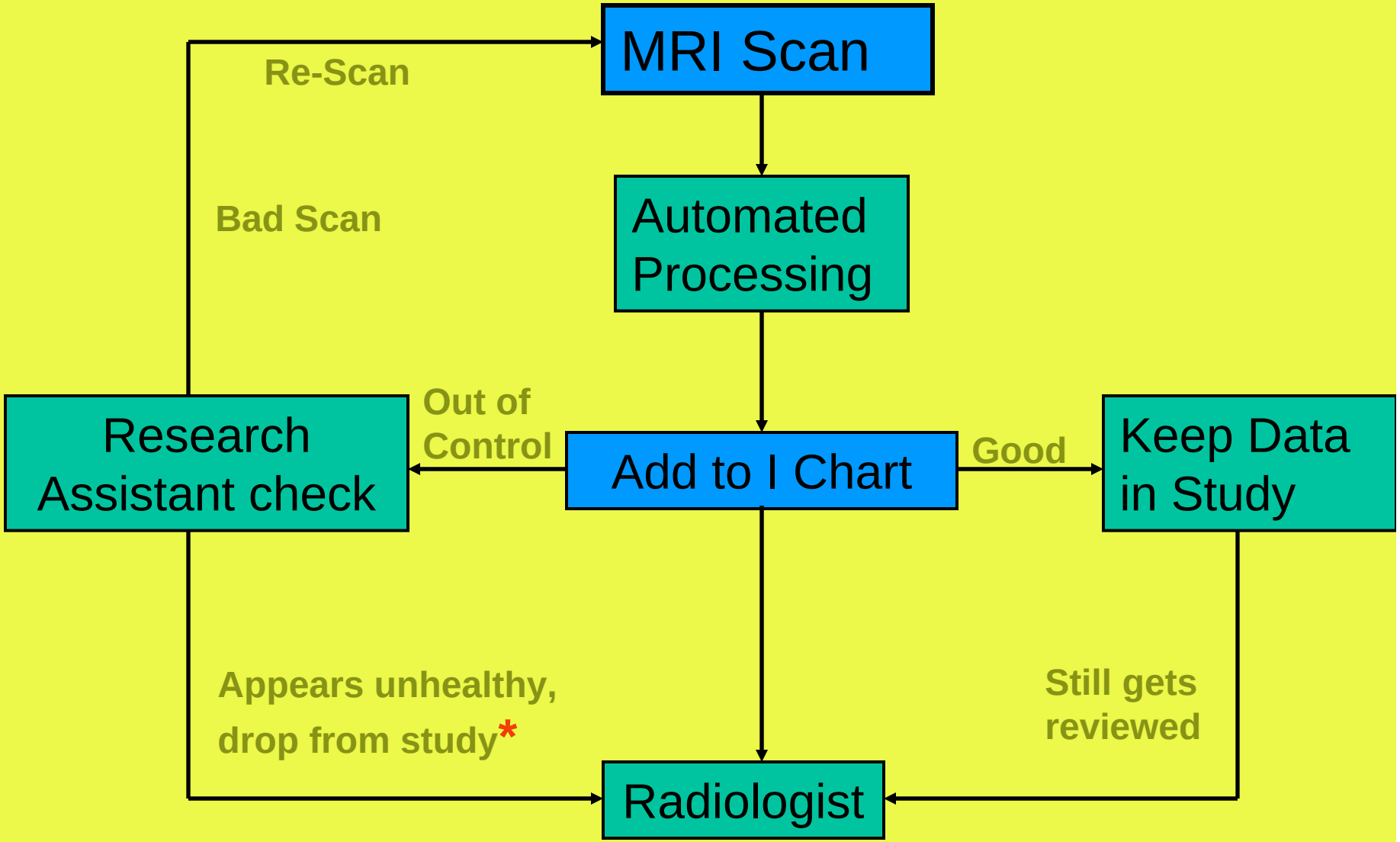
Overview:

- Current Practice
- Physics of MRI and the T1 Image
- Quality Control in MRI
- Example of Using individuals Chart with Morphological Data
- Reasons for researching use of Process Control Charts in Clinical Data
- Moving forward

Flow Chart (current)



Flow Chart (future)



***Subjects that are screened as healthy but appear unhealthy are the ones that can be dropped at PI discretion**

Background on Federally Funded Grants and Ethics

- All grants must go through IRB approval
- All subject's brains will be reviewed by a radiologist
- In Health Sciences, subjects must be screened for health problems related to the study
- QA flags those most likely to have health problems to get screened first
- This is NOT a substitute for human reviews

Current Practice

- Screen patients using questionnaires with no structural follow-up

- What if a healthy control is really not healthy?

The Unhealthy Healthy Control

Consequences:

Changes what researchers think they are comparing

Could increase variability among healthy subjects

Could lessen effect size differences between patients and controls

A brief History of MRI

Resonance was discovered by I.I. Rabi

He used an oscillating magnetic field to detect resonance in a molecule

Dr. Felix Bloch of Stanford postulated that a charged particle with spin would produce a magnetic field

Dr. Purcell, Dr. Torrey, and Mr. Pound detected resonance in paraffin (solid state resonance)

A brief History of MRI

Many other people added to the science so that images could be produced.

Dr. Damadian was the first to publish that cancerous cells had longer T1 relaxation times

Dr. Paul Lauterbur and Sir Peter Mansfield were awarded the 2003 Nobel Prize in Physiology or Medicine

T1 relaxation

An initial magnetic (B_0) field is applied to the brain

The hydrogen molecules line up parallel or antiparallel to the field

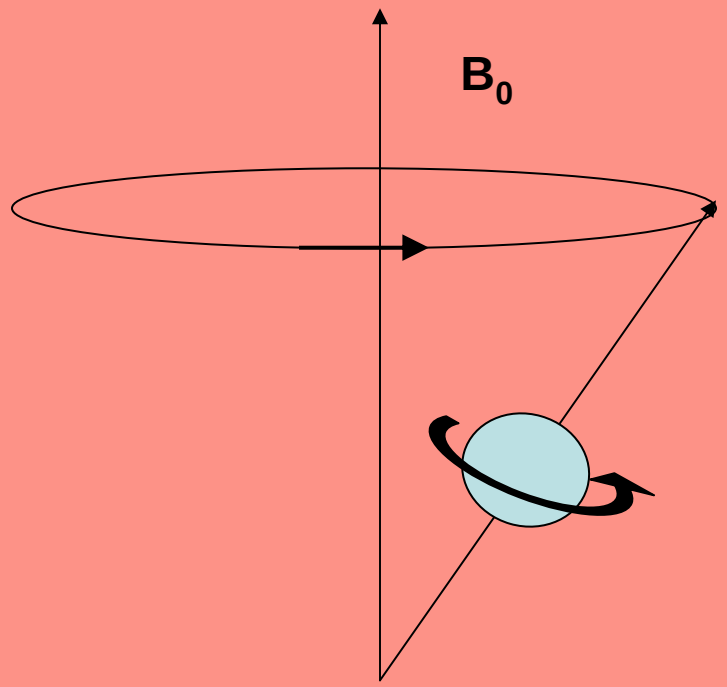
A radiofrequency pulse (RF) close to the Larmor frequency is applied

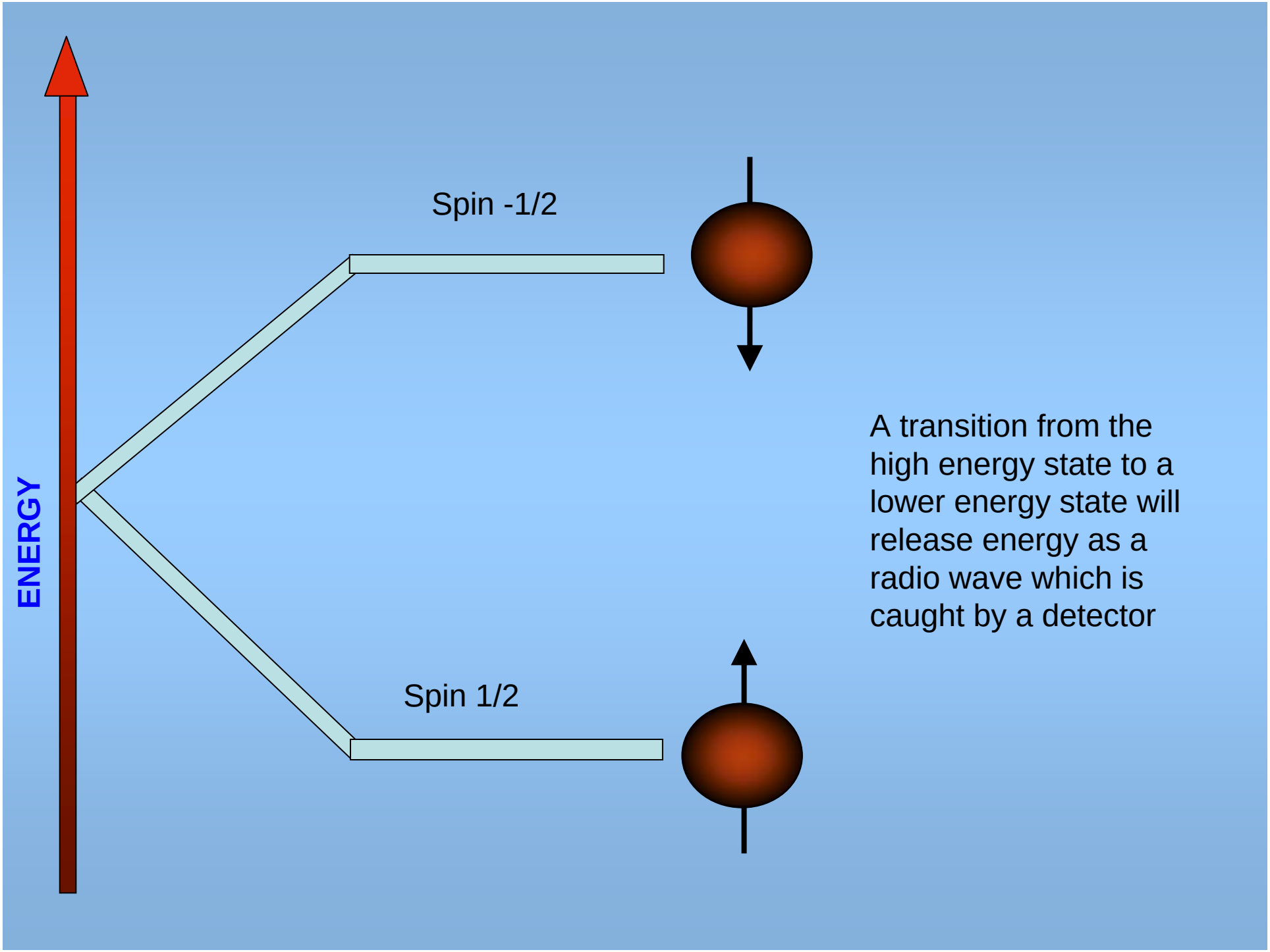
The oriented protons are perturbed into a higher energy state

The recovery to a lower energy state follows the Bloch Equation:

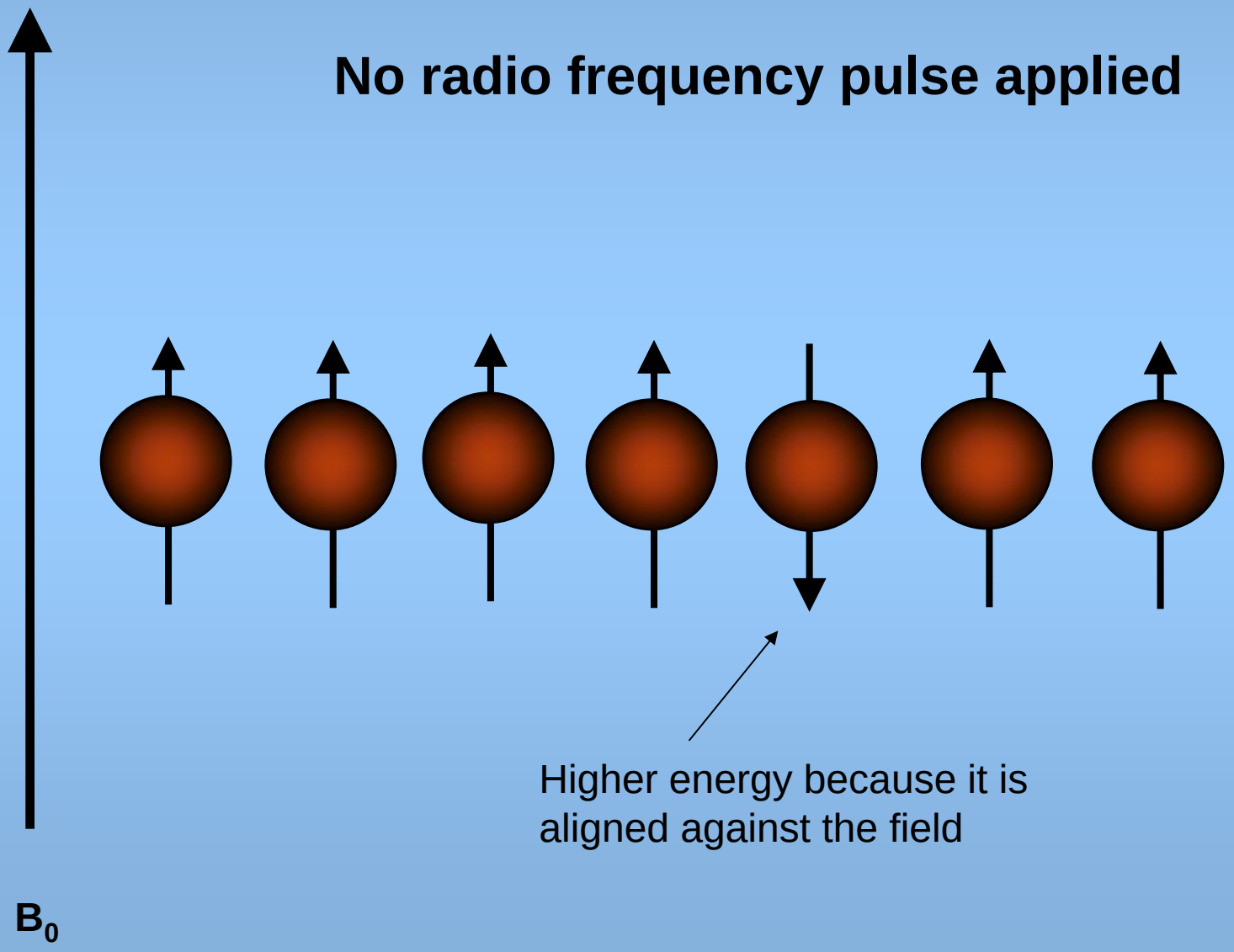
$$\frac{dM_z(t)}{dt} = \frac{M_0 - M_z(t)}{T_1}$$

Proton in an applied Magnetic field



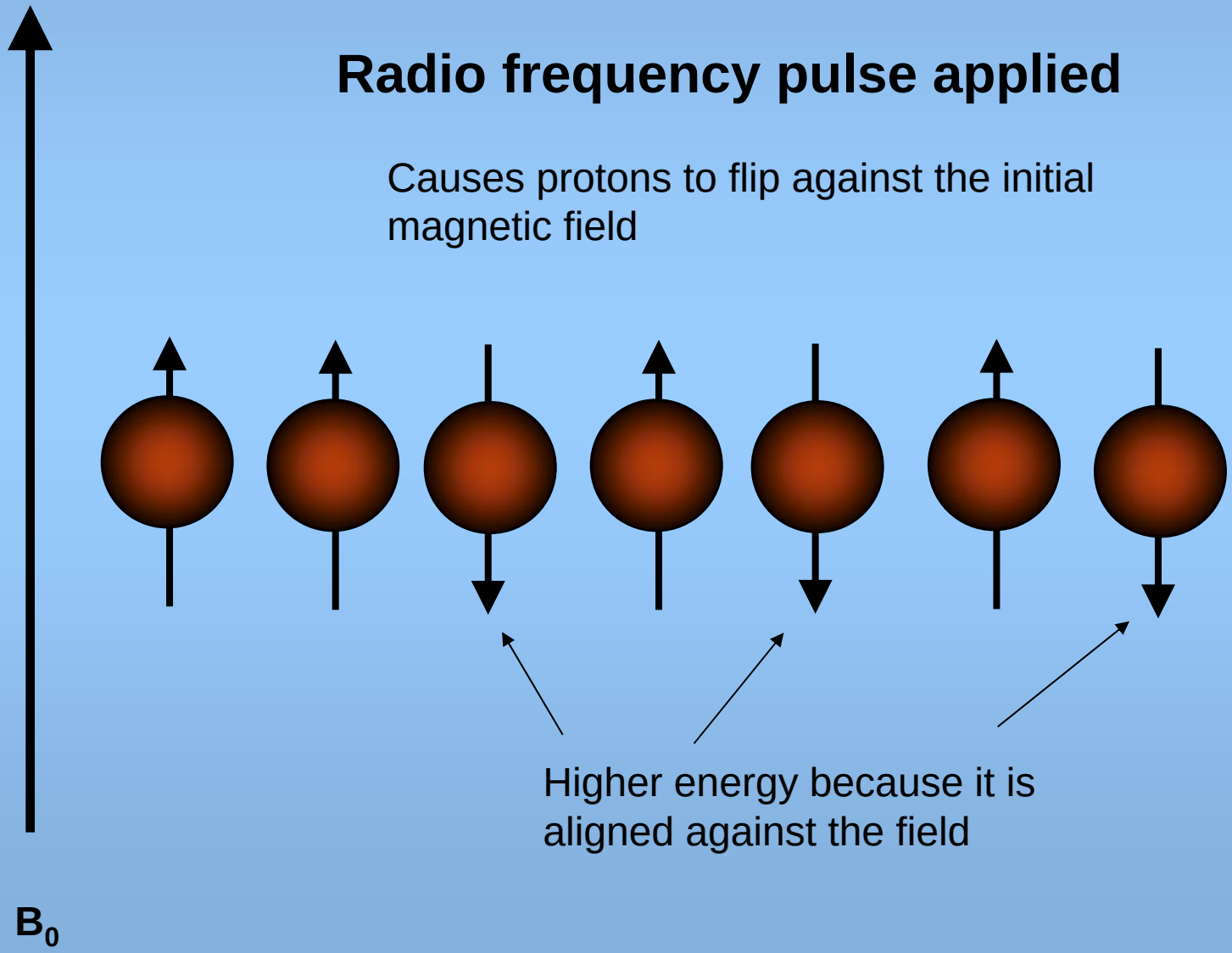


A transition from the high energy state to a lower energy state will release energy as a radio wave which is caught by a detector

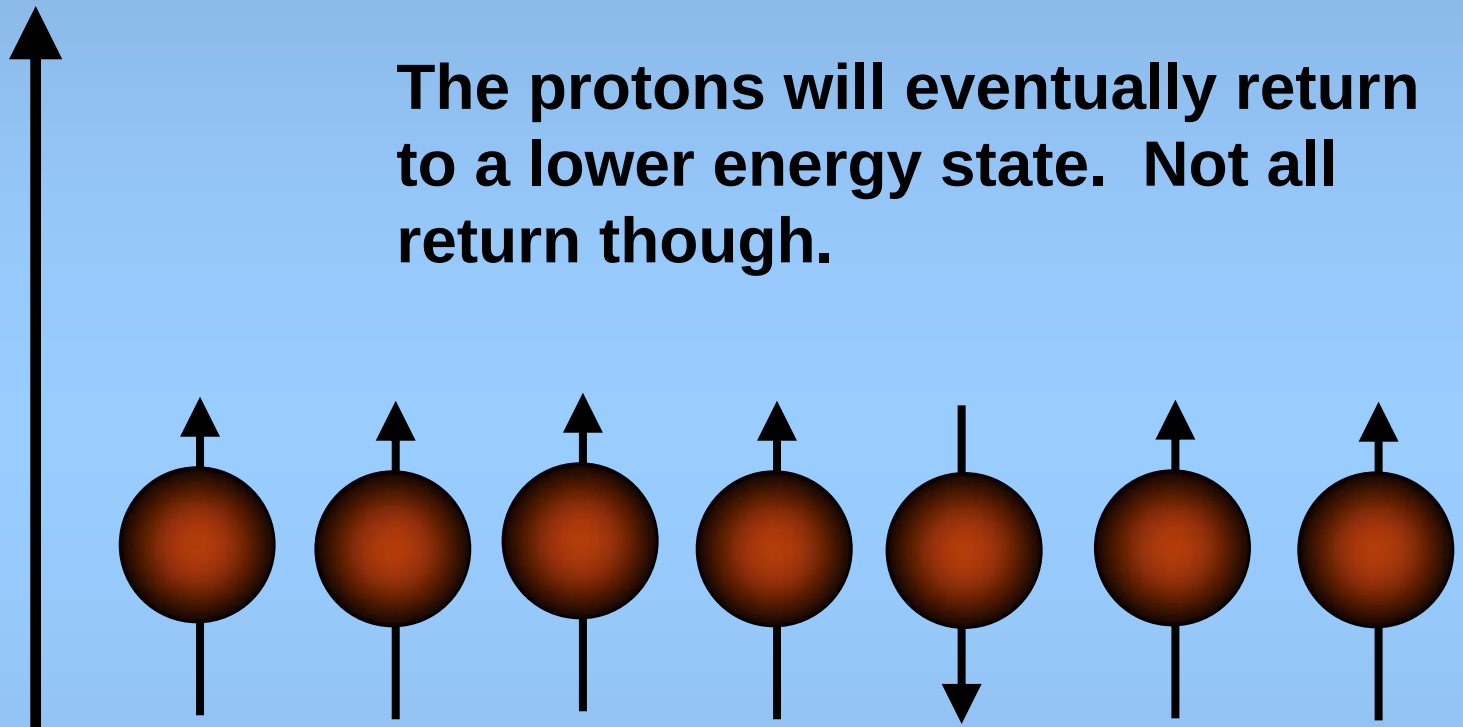

No radio frequency pulse applied
Higher energy because it is aligned against the field
B_0

Radio frequency pulse applied

Causes protons to flip against the initial magnetic field



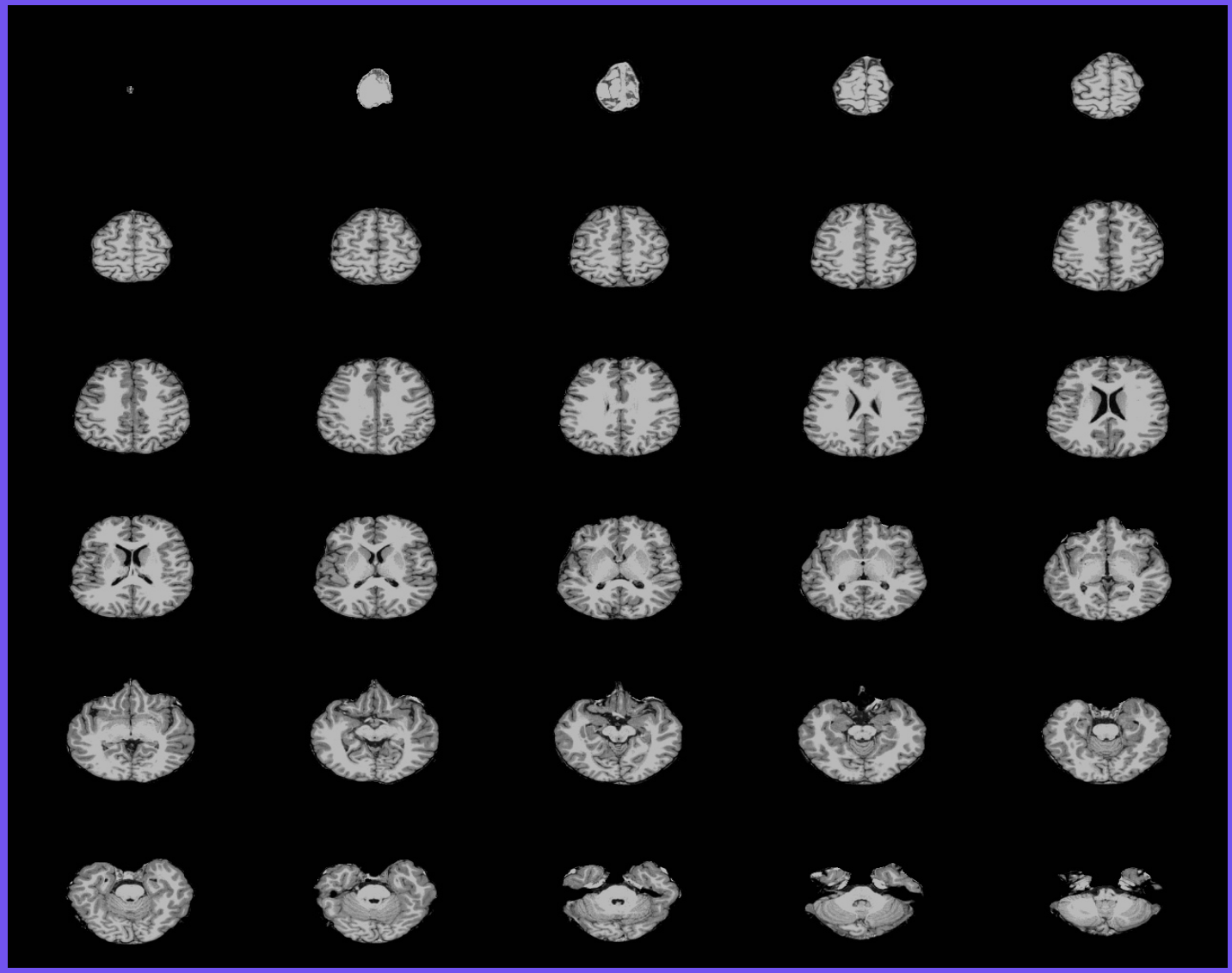
The protons will eventually return to a lower energy state. Not all return though.



Higher energy because it is aligned against the field

B_0

A Sample T1 Image of a Brain



T_1 and Physiology

Pure water is not affected by magnetic field strength

The relaxation time for T_1 of water is the same at 1.5T as it is at 3T

Physiology (particulate masses) make T1 different among structures

Pathology makes a difference too

Quality Assurance in MRI

Any of the following can cause measure error

- Slice Thickness accuracy
- Radiofrequency coils
- Software issues
- Non-ideal slice profile
- Magnetic Field Homogeneity
- Radiofrequency Pulse amplitude

Controlling the Quality of the Scanner

Keeps measures accurate over time

Allows for reproducibility

In the future it may allow for multi-site comparisons

http://www.uvm.edu/~cnru/fbip/scanner.jpg

Summary of Methods

We used the Harvard based package **FREESURFER** to parse out structures in the brain using the freesurfer atlas

Website:
https://surfer.nmr.mgh.harvard.edu/fswiki/FreeSurferAnalysisPipelineOverview

The structures were volume measured and the volumes were quality checked in SAS

Data Description

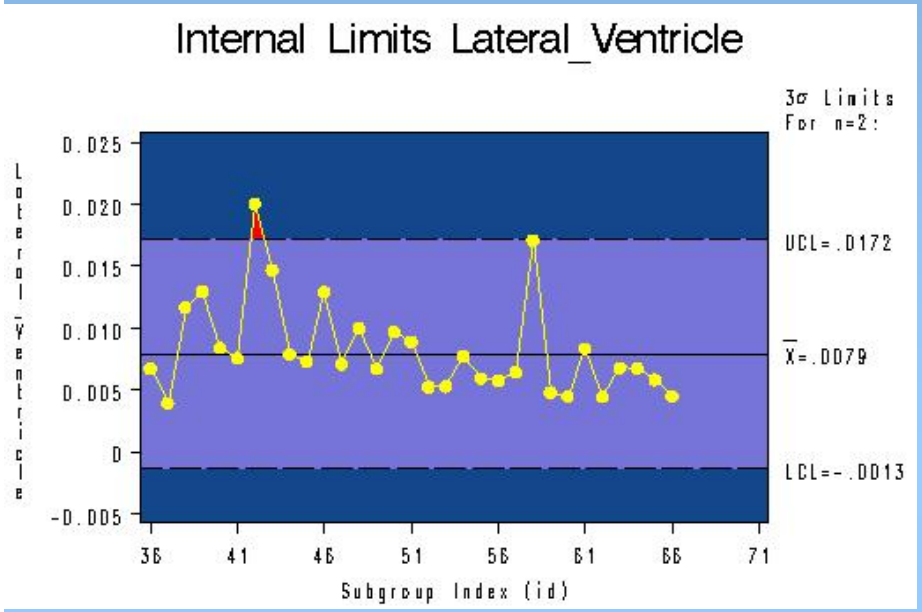
66 subjects from New Mexico were given T1 brain scans

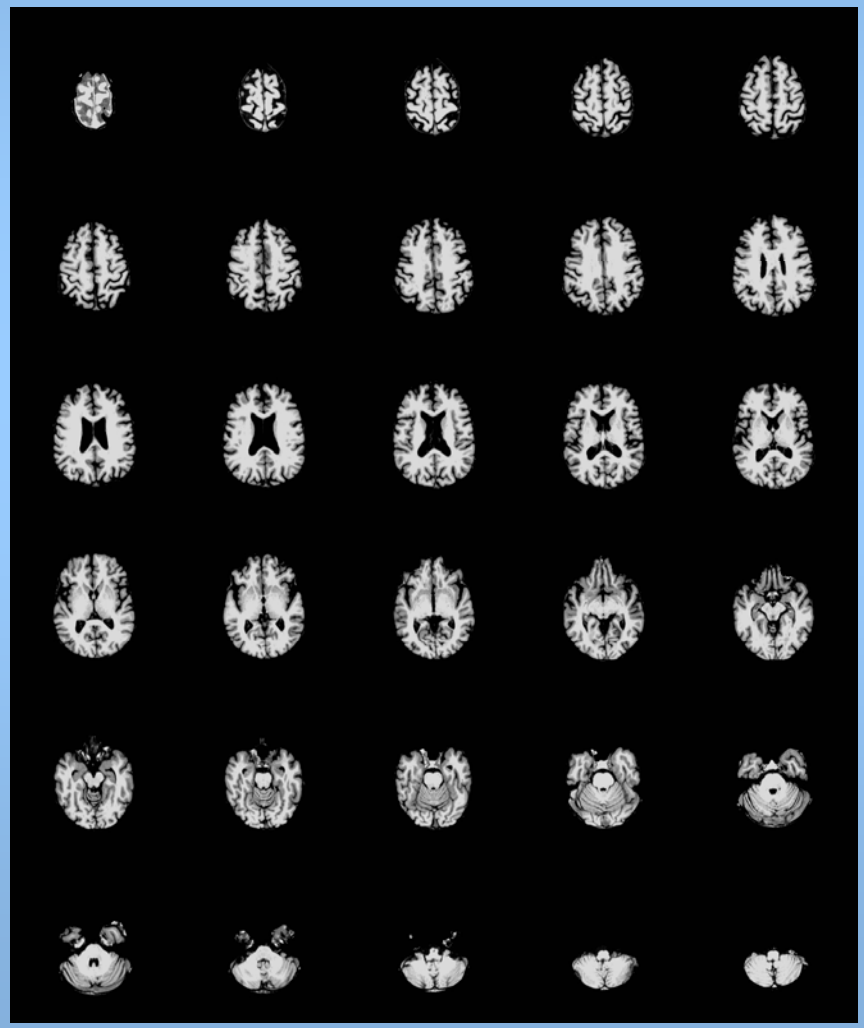
Each T1 brain scan can be 16M in size

Voxel resolution is

1mm X 1mm X1mm

EXAMPLE





Subject with ventricles statistically larger than sample

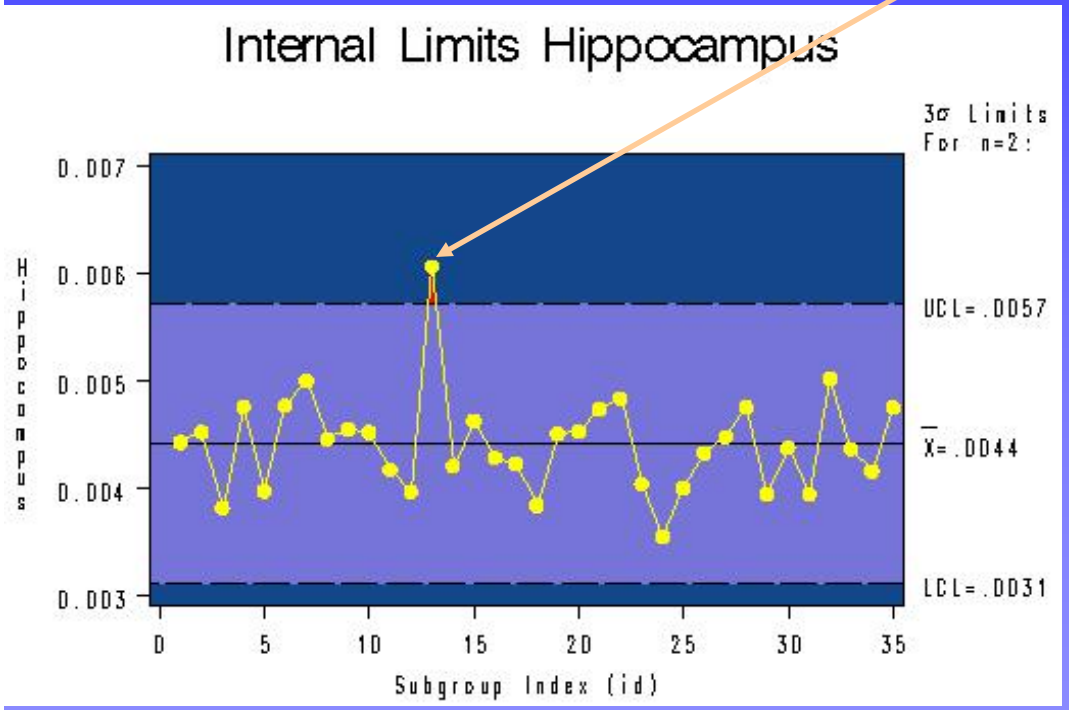
Except this is a chronic patient and large ventricles are to be expected

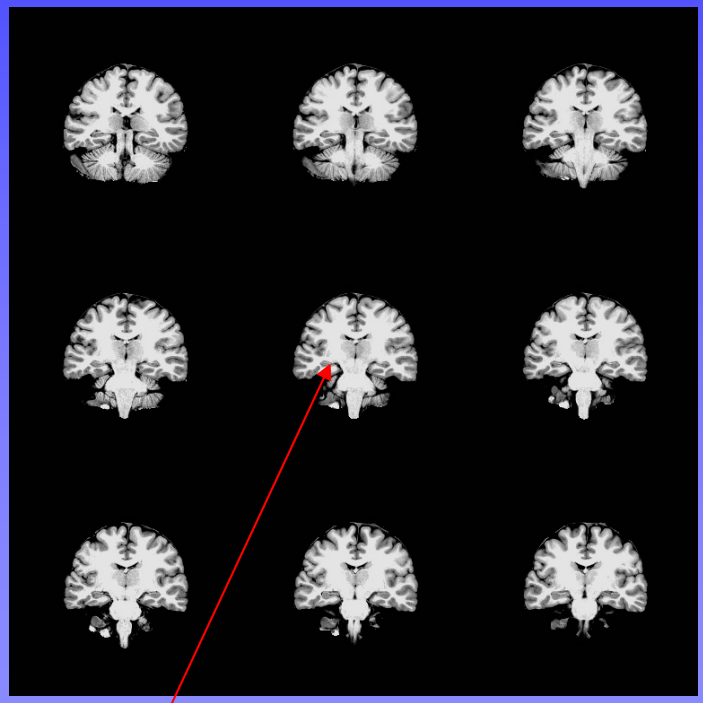
This only confirms what was anticipated

CAN A HEALTHY PERSON BE OUT OF CONTROL?

YES

Healthy Subject





Hippocampus is in this region

Data Dictionary

Subject Type:

First Episode Patient, First Episode Control, Chronic Patient, Chronic Control

Region:

Thalamus Proper, Putamen, Pallidum, Lateral Ventricle, Inferior Lateral Ventricle, Hippocampus, Cerebral White Matter, Cerebral Cortex, Cerebellum White Matter, Cerebellum Cortex, Caudate, Amygdala, Accumbens area

Level of Failure:

They can either be at or outside of control limits

Table of Subjects Caught Out of Control

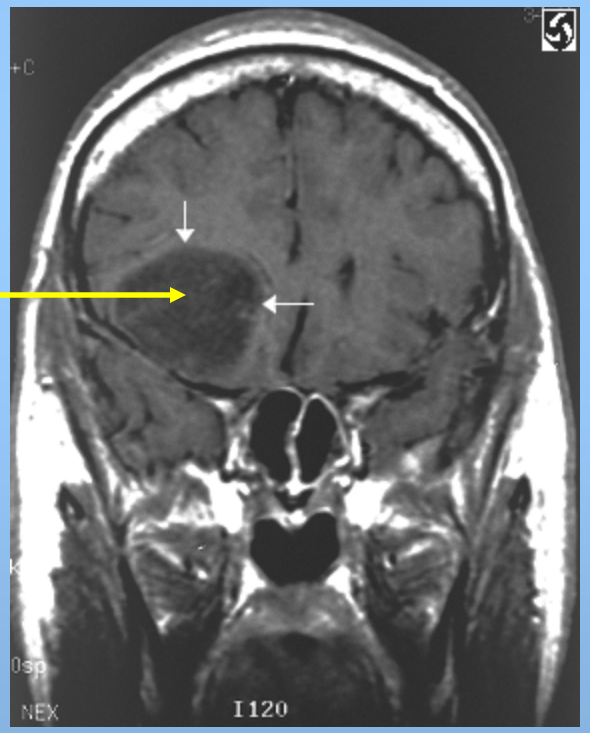
Subject Type	Subject ID	Region	Level of Failure
First Episode Patient	41	Accumbens area	Above UCL
Chronic Patient	54	Amygdala	At UCL
Chronic Patient	31	Caudate	Above UCL
First Episode Patient	7	Cerebellum White Matter	At UCL
Chronic Control	13	Hippocampus	Above UCL
Chronic Patient	42	Inferior Lateral Ventricles	Above UCL
Chronic Patient	43	Inferior Lateral Ventricles	Above UCL
Chronic Patient	42	Lateral Ventricles	Above UCL
First Episode Patient	31	Putamen	At UCL

Individual Measures Chart

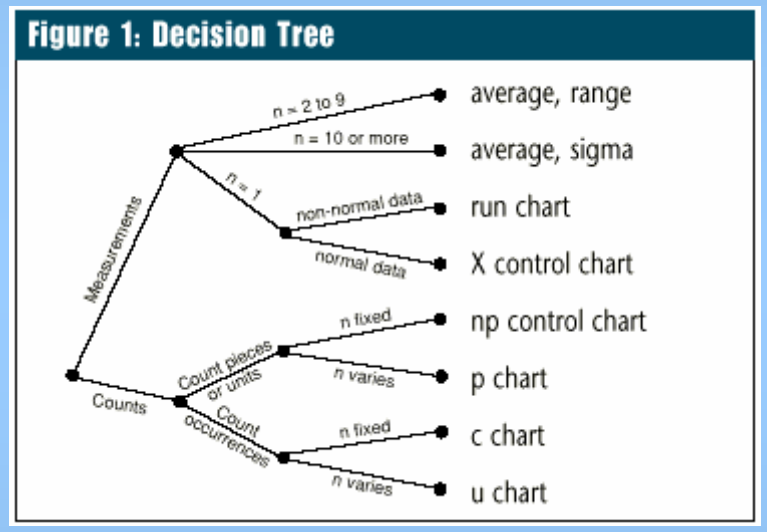
No Range Chart is used because subject ordering is nonsensical

Intended to detect one of three things:

Unhealthy brains



http://brighamrad.harvard.edu/Cases/bwh/images/49/DR10MRT1A.GIF



http://www.qualitydigest.com/feb98/html/spctool.html

Individual Measures Chart

Bad Images

Individual Measures Chart

Poor software processing of the brain

Current Work

Use a larger national database such as Dr. Dave Kennedy's* to estimate the mean, UCL, and LCL values of brain volumes from multiple sites/studies

This would decrease variability (hopefully) and give greater confidence in estimated volumes

* http://www.cma.mgh.harvard.edu/ibvd/

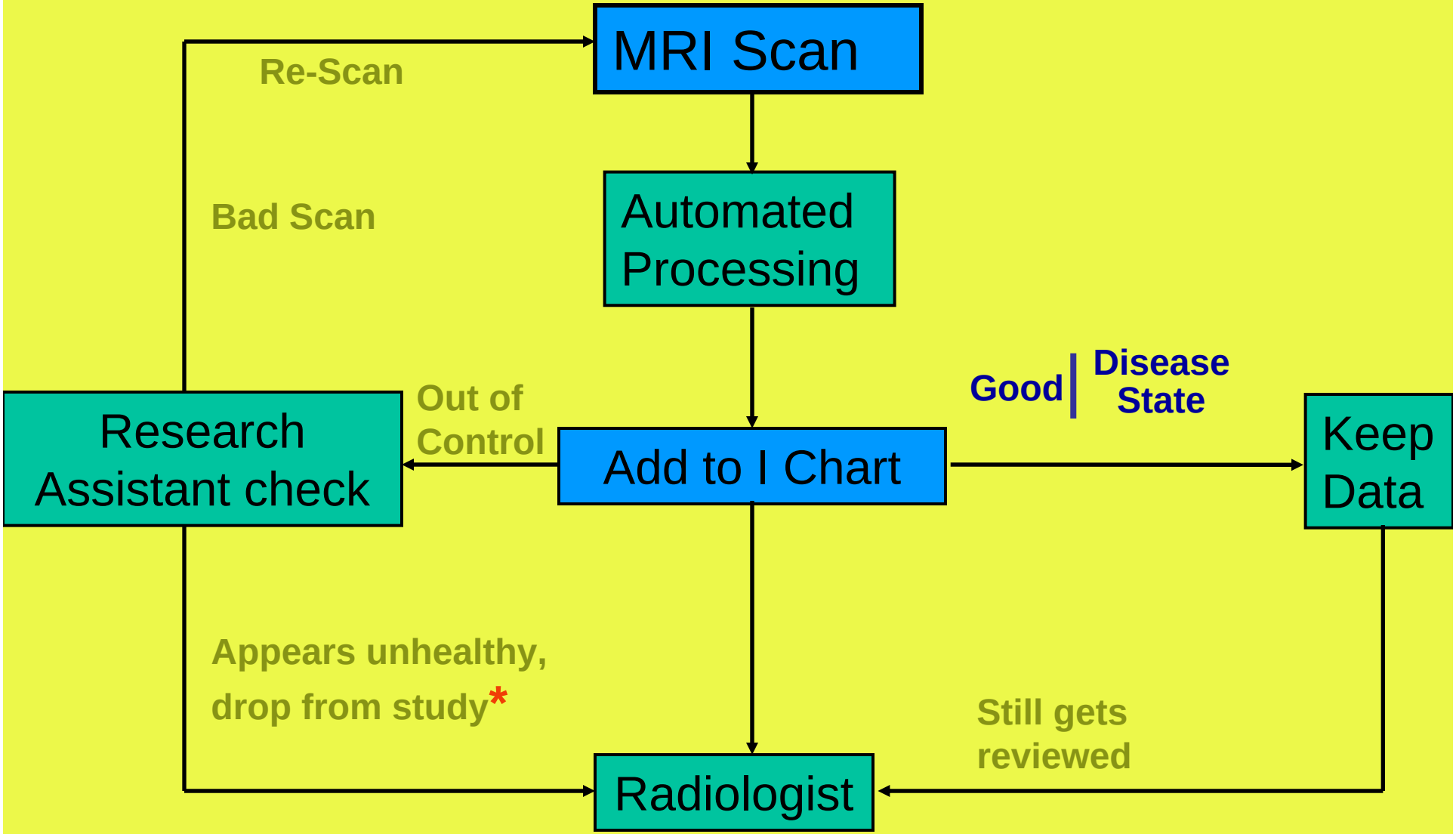
Current Work

Use only subjects from a specific disease state to detect outliers

This should make the control charts more sensitive to outliers

It would decrease variability because it is known that certain disease processes show volume differences

Flow Chart (future)



***Subjects that are screened as healthy but appear unhealthy are the ones that can be dropped at PI discretion**

Current Work

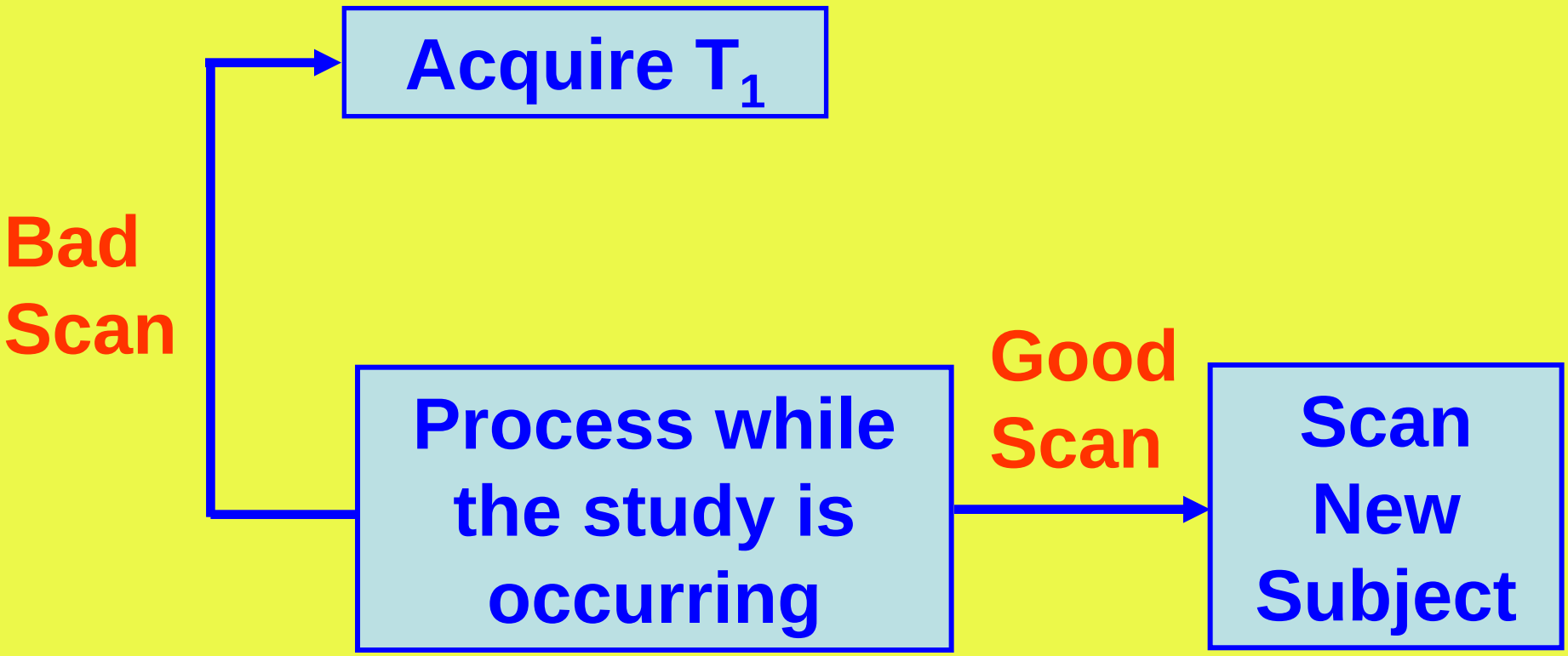
Automate the process

It takes about 8 minutes to get a T_1 scan

A study can be up to 3 hours in length

A brain can be processed in 30-60 minutes

Flow Chart for Automation



Potentials

As scanners become faster and are able to take smaller slices of the brain, the radiologist will be overwhelmed

Control charts based on automated measures can direct the radiologist to potential problem areas

Control Charts can also be used to track lesion or tumor growth over time

A Special Thank You to:

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