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MEDICINE

RADIATION ONCOLOGY &
MOLECULAR RADIATION SCIENCES

Medical Software: A Clinical and Commercial Perspective

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To provide a general idea of the processes and issues related to developing Medical Software

- Review Product Development Process

- Simplified TPS/IMRT product example

Concerns about Medical Software Development

- Safety, Safety, Safety
- Highly specialized
- Smaller market -> higher dollar
- Interoperability (customers demanding standards – DICOM)
- Tendency to package software developed in a academic or research setting
- Cutting corners may improve time to market, but…
  - Infrastructure – longevity…
  - Usability…
  - Support…
  - Safety…
- FDA understands, but cannot afford to police product safety
  - FDA police Development Process as it is common across industry
  - Lack of knowledge of each product prevents policing safety directly.
  - Safety is monitored as product is used.
    - Incident reports are required by law to be reported by industry to FDA when they occur.
    - Website publishes them. http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/search.CFM

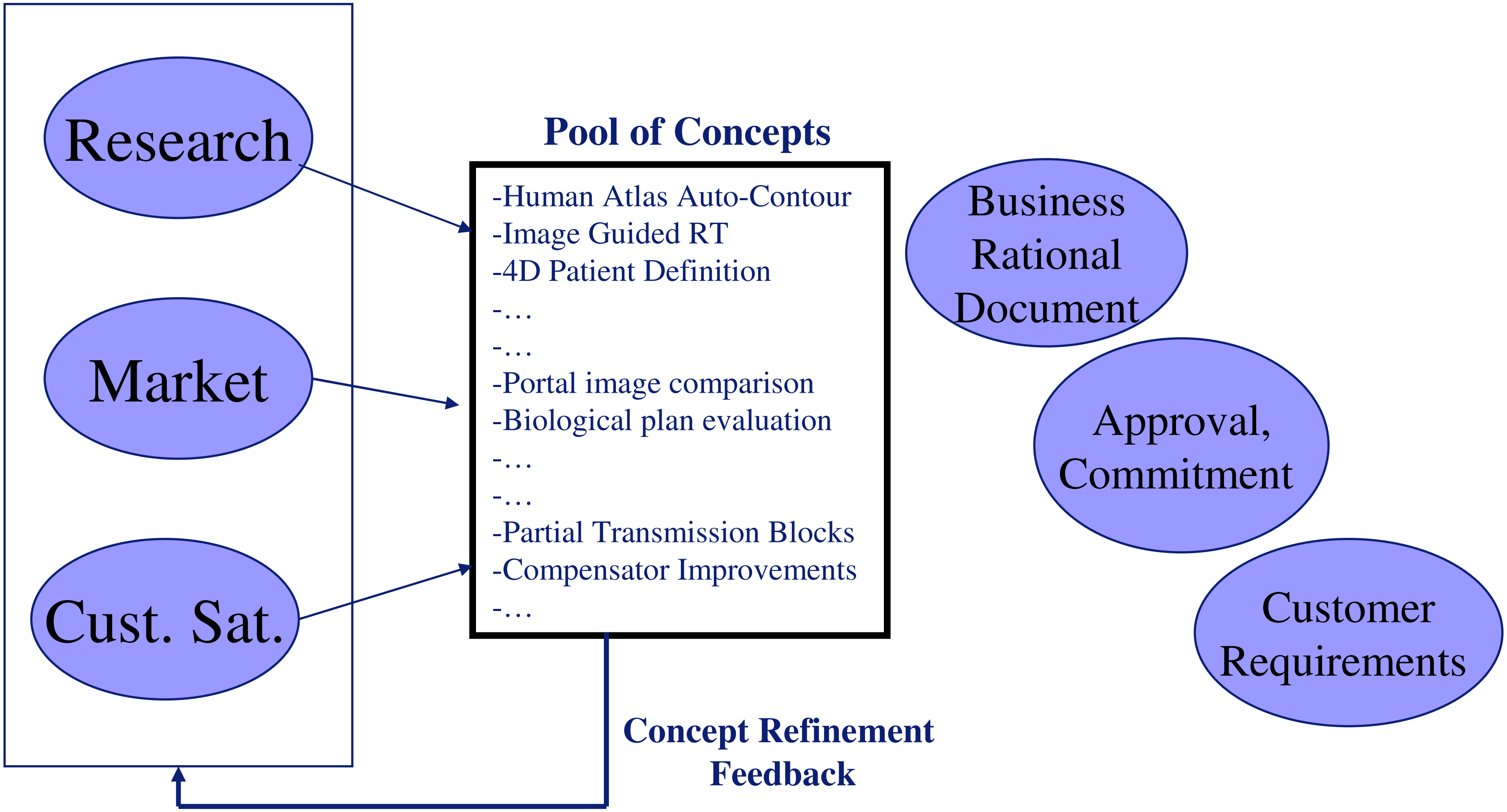
Quality System

- All manufactures of medical devices must maintain a quality system
- Quality system is audited periodically
  - Required for FDA, CE Marking
  - ISO-9000 certification is independent of regulation but similar
- Quality system defines standard operating procedures (SOP) for a development organization
- SOP cover Product specifications through design, support and complaint handling.
- FDA 510K approval requires documented evidence that your quality system was followed in the product development
  - It does not guarantee that the product is safe.

FDA - 21 CFR Part 820

- Quality System Requirements
  - Audit policy
  - Personnel training
- Design Controls
- Document Control
- Identification and Traceability
- Production and Process Control
- Corrective and Preventative Action (CAPA)
- Labeling and Packaging
- Records
  - Device Master Record
  - Device History Record

Product Conceptualization



Research

Market

Cust. Sat.

Pool of Concepts

-Human Atlas Auto-Contour
-Image Guided RT
-4D Patient Definition
-…
-…
-Portal image comparison
-Biological plan evaluation
-…
-…
-Partial Transmission Blocks
-Compensator Improvements
-…

Concept Refinement Feedback

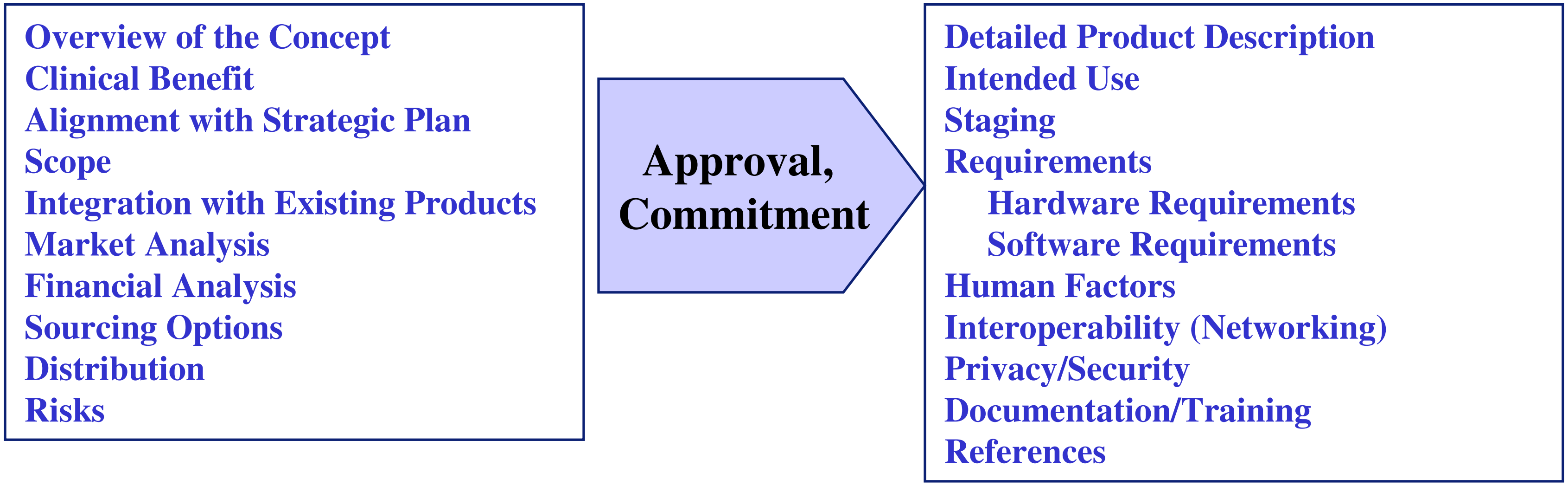
Business Rational Document

Approval, Commitment

Customer Requirements

Business Rationale

Customer Requirements



Overview of the Concept
Clinical Benefit
Alignment with Strategic Plan
Scope
Integration with Existing Products
Market Analysis
Financial Analysis
Sourcing Options
Distribution
Risks

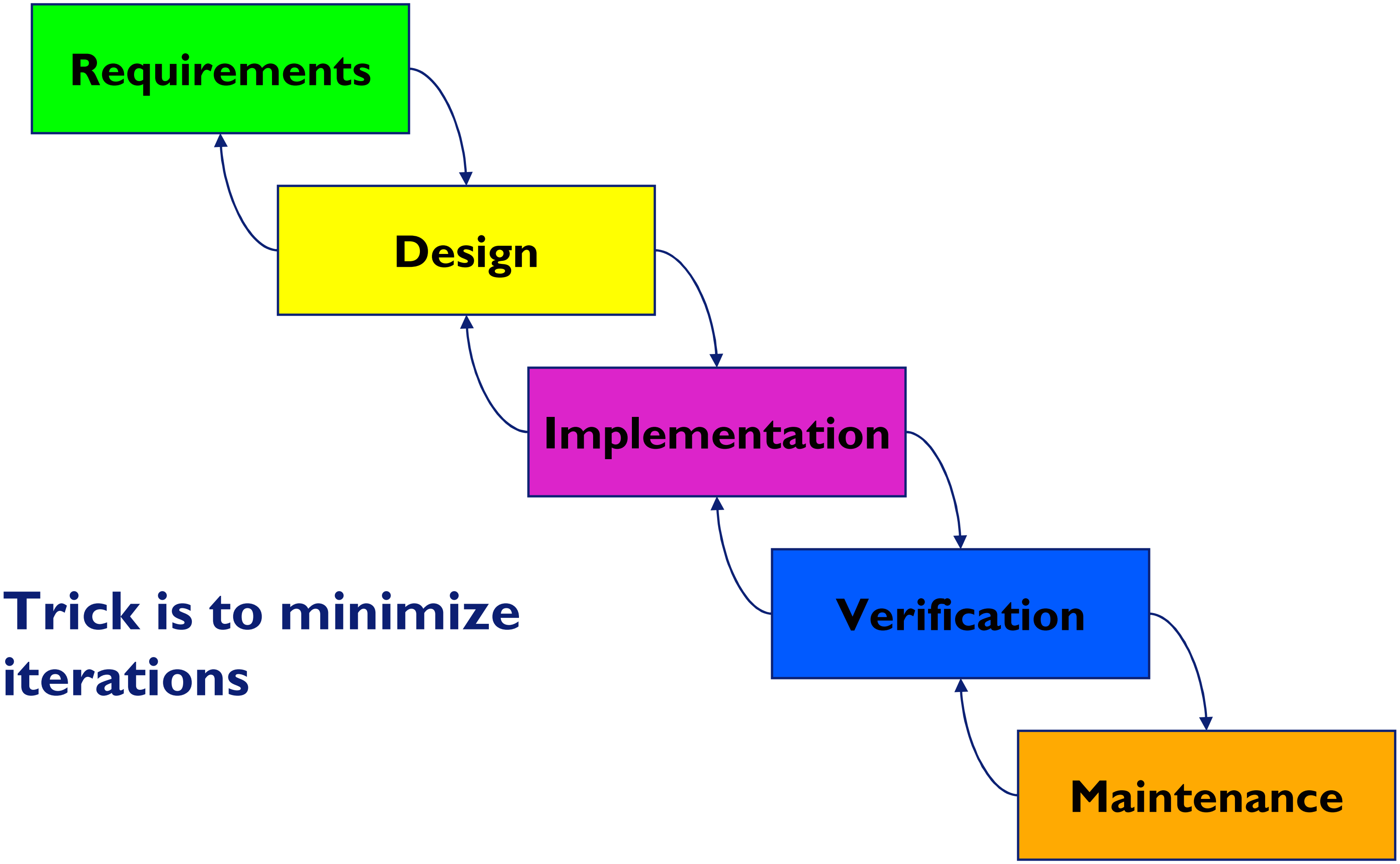
Approval, Commitment

Detailed Product Description
Intended Use
Staging
Requirements
    Hardware Requirements
    Software Requirements
Human Factors
Interoperability (Networking)
Privacy/Security
Documentation/Training
References

Approval and Commitment Considerations:

- Market potential
- Return on investment
- Alignment with Strategic Plan
- Scope to completion
- Competitive advantage
- Customer satisfaction
- Availability of resources
- Feasibility
- Categorization Metrics

Modified Waterfall Development Process



Trick is to minimize iterations

Customer Requirements Specifications

- Typically owned by “Marketing”
- You are not the end customer!
- What can the customer use? (minimum viable product)
- Use cases
  - Several scenarios on how the product will be used
- Detailed list of specifications
  - e.g. User must be able to specify treatment objectives for a set of defined structures
- Performance requirements
  - e.g. Dose computation speed
- Backward compatibility
- Interoperability requirements
- Installation and support requirements

Software Requirements Specification

- Engineering response to customer requirements
- Detailed list of software specifications
  - e.g. System must allow the user to identify a treatment objective…
    - By graphically moving an icon on a DVH display with the mouse
    - By typing dose and percent volume levels into a spreadsheet form
- Use of standards
- Network linkage
- Database
- Verification testing strategy
- User documentation

Risk Analysis and Mitigation

- Risk analysis against specifications
  - Brainstorm of all potential safety risks
- Score the risks based on
  - Detectability (experience user)
  - Severity (death, injury)
  - Probability of occurrence (for software usually 100%)
- Mitigate risk through software specification, design, and documentation.
  - The dreaded warning message should be the last resort
- Risks must be mitigated below level specified by your process

Repeat Statements to AVOID

Nobody would ever want to do that.

They will never load a data set that big.

This bug rarely occurs.

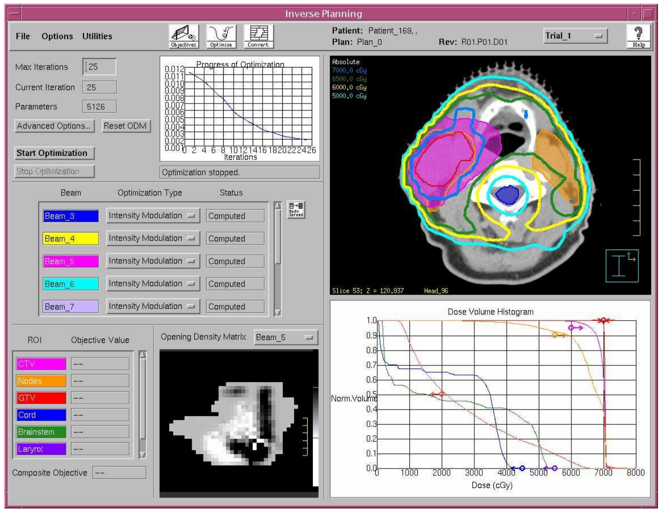
The other system will catch that.

Statement to remember:

If it can happen, it will!

Software Design Document

- Detailed design of the software to be developed
- Object hierarchy - Unified Modeling Language (UML)
- Software Interfaces
- Human Interface Design
- Module testing strategy



Patient: Patient_169, ,
Plan: Plan_0
Rev: R01.P01.D01
Trial_1

Max Iterations 25
Current Iteration 25
Parameters 5126

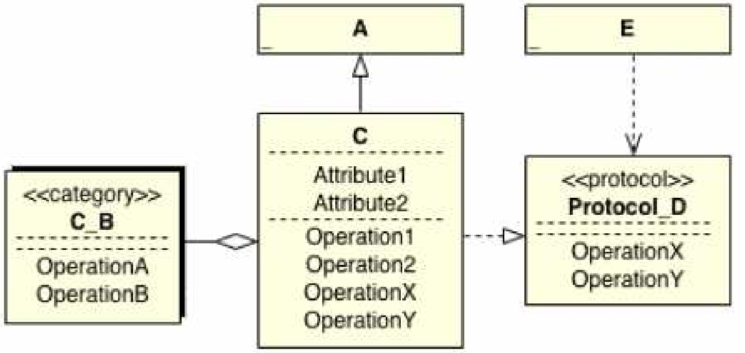
Optimization stopped.

Beam	Optimization Type	Status
Beam_3	Intensity Modulation	Computed
Beam_4	Intensity Modulation	Computed
Beam_5	Intensity Modulation	Computed
Beam_6	Intensity Modulation	Computed
Beam_7	Intensity Modulation	Computed

ROI	Objective Value
CTV	--
Nodes	--
GTV	--
Cord	--
Brainstem	--
Larynx	--

Composite Objective --

Opening Density Matrix Beam_5



UML Class Diagram for Objective-C Constructs

Architecture Concerns

- Modular design
  - Allows for module testing to limit scope of required testing
  - Allows for focused integration testing to avoid repeat testing of large portions of the application for small corrections.
  - Allows for the incorporation of 3rd party components
- Larger companies are trying to build common framework
  - Centralized group building software components to medical products
  - Standard image processing and display tools
  - DICOM support structure
  - Standardized Graphical User Interface requirements

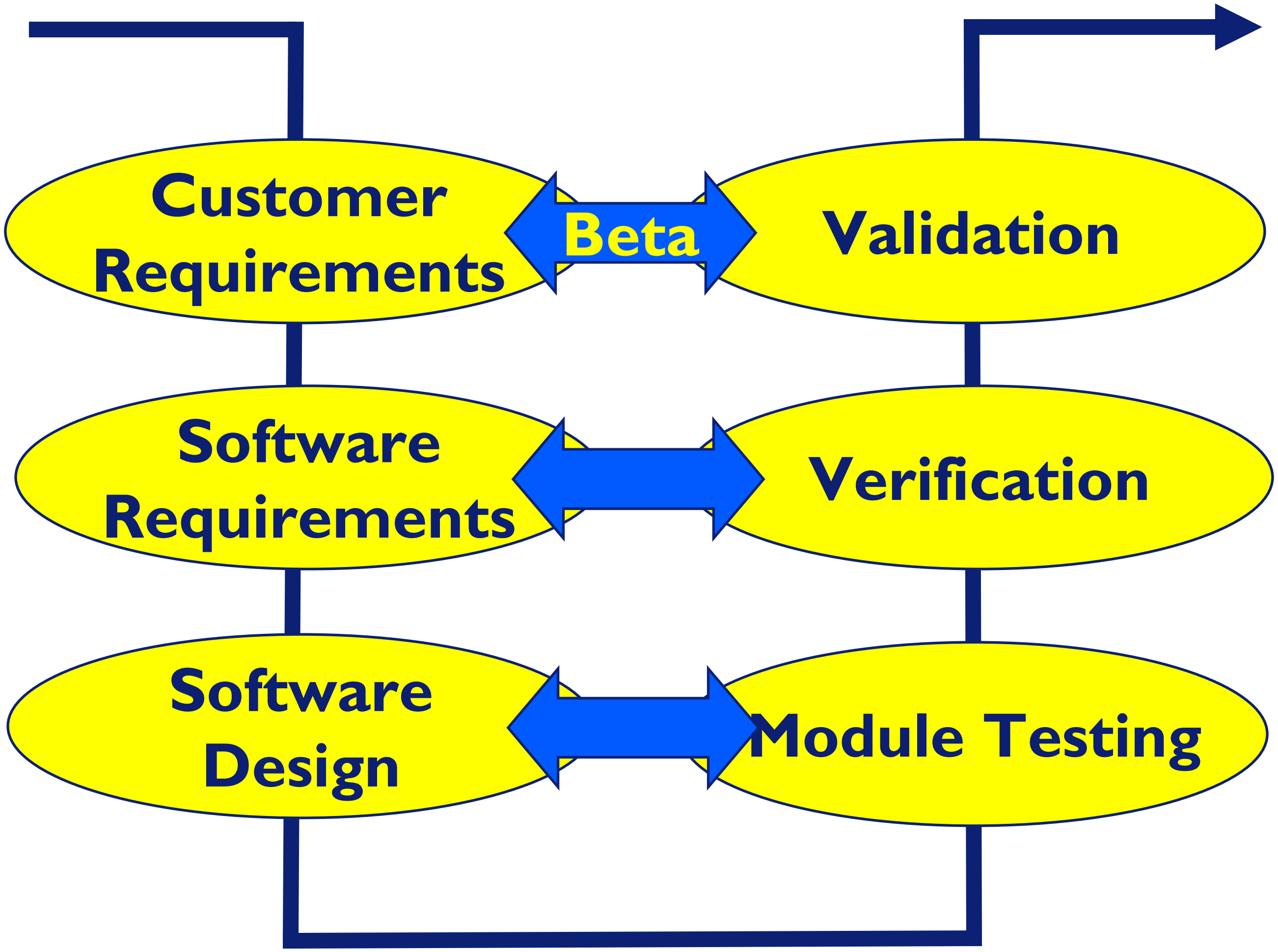
Coding Standards and Revision Control

- Standardized Notation
  - Improves readability for other coders
  - e.g. Hungarian Notation

```
float fCalculateArrayMean(void *pvDataArray, int iNumberOfData){
          float fMeanValue = 0.0;
          int iIterator;
          for(iIterator=0; iIterator < iNumberOfData; iIterator++)
                    fMeanValue += (float)pvDataArray[iIterator];
          fMeanValue /= (float)iNumberOfData;
          return(fMeanValue);
}
```

- Comments – new tools enable auto documentation (JavaDoc)
- Test functions for module testing
- Revision control
  - Checkin process
  - Documented code review

Software Development Verification



Release

User docs
Support training
Packaging
Distribution
Installation

- **Module (Unit) Testing**
  - Testing of individual code modules
  - Usually automated
  - Owned by engineering
- **Verification (Integration) Testing**
  - Development and execution of detailed test plans
  - Traceable to items in the SRS
  - Owned by QA department
- **Validation (Beta) Testing**
  - Validation that software meets intended use
  - Traceable to items in the CRS
  - Owned by QA and Marketing

Complaint Handling

ANY communication indicating a potential defect

- Manufacturer must have a procedure for receiving, reviewing and evaluating complaints
- All employees of company are responsible for reporting
- Complaints are assessed for severity
- Patient safety complaints are required to be reported to the FDA
- High severity defects require Corrective And Preventative Action (CAPA)
  - Process modification for prevention
  - Field notification and/or modification
  - Product Recall

Really Simplified Treatment Planning and IMRT Example

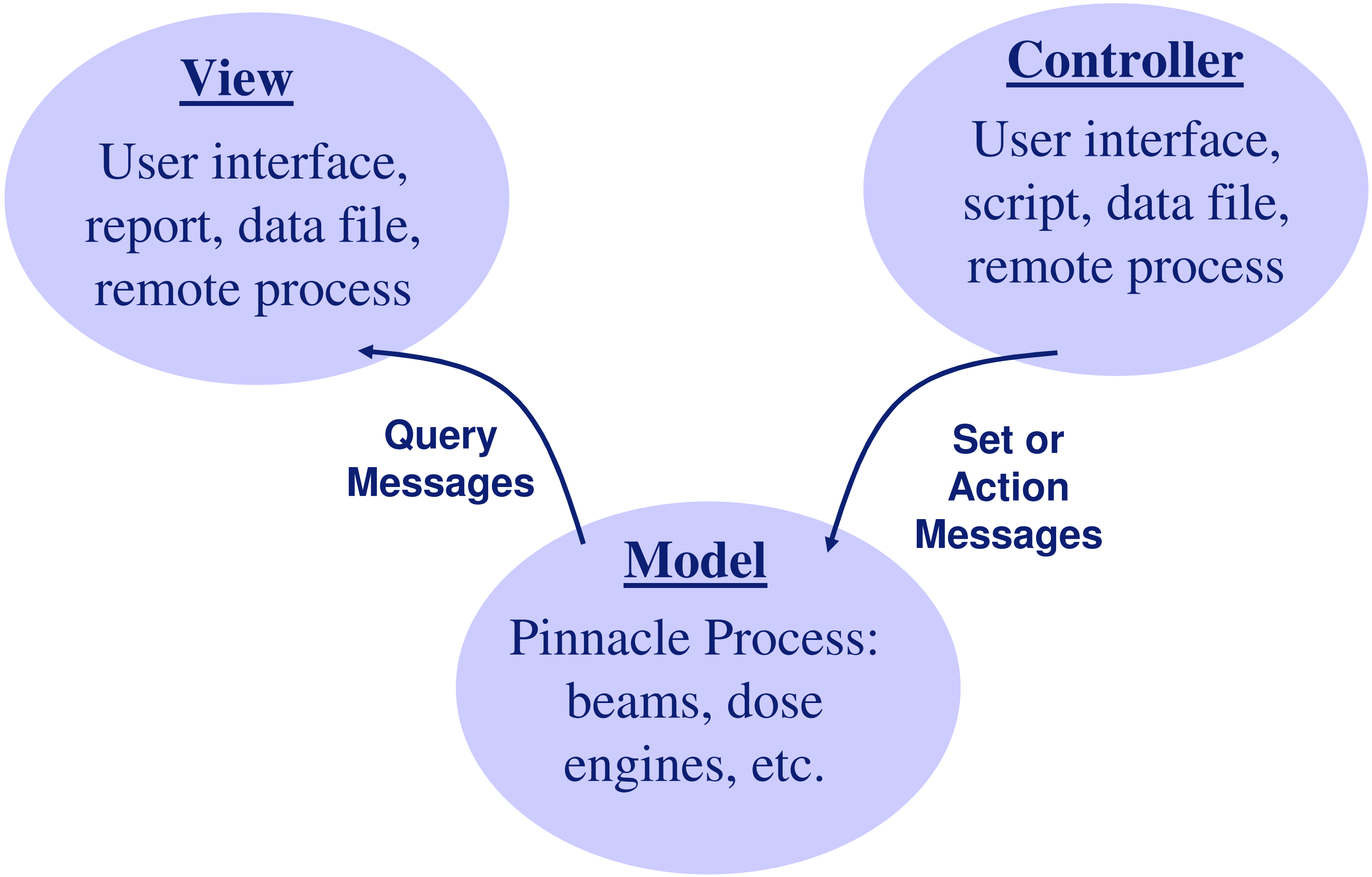
Customer Requirements (IMRT)

- Use cases…
- Must integrate with existing TPS
- User must be able to…
  - Specify treatment objectives for a set of defined structures
  - Optimize Tx parameters to meet specified objective
  - Optimize parameters for a subset of beams while keeping other beam(s) the same
  - Allow the optimization of beam weight for one beam and intensity modulation for another
- Performance requirements
  - Plan typical treatment in 10 minutes start to finish
  - Iterative dose computation must not require independent commissioning
- Quality Assurance tools
  - User must be able to:
    - Transfer plan to a standard phantom
    - Compute dose to flat water phantom at specified depth
    - Export dose information to dosimetry systems
- Plan Export
  - The treatment plan must be able to be exported to record and verify systems

Risk Analysis and Mitigation (IMRT)

- System fails to send MLC information or sends incorrect MLC patterns to Linac
  - Severity (high), Detectability (Low)
  - Mitigation thru documentation
    - Document need to perform IMRT QA for each patient
    - Document acceptance testing to verify proper transfer of MLC leaves
- System uses incorrect CT to density table for dose computation
  - Severity (medium to high), Detectability (low)
  - Mitigation through software
    - Allow users to specify which CT to Density tables can be used for dose computation
    - Document in User Docs
- System generates excessively high beamlet intensity
  - Severity (potentially high), Detectability (medium)
  - Mitigation
    - Display isodose curves
    - Display maximum dose to defined structures
  - Is it really mitigated???

Pinnacle^3 M-V-C Architecture



View

User interface, report, data file, remote process

Controller

User interface, script, data file, remote process

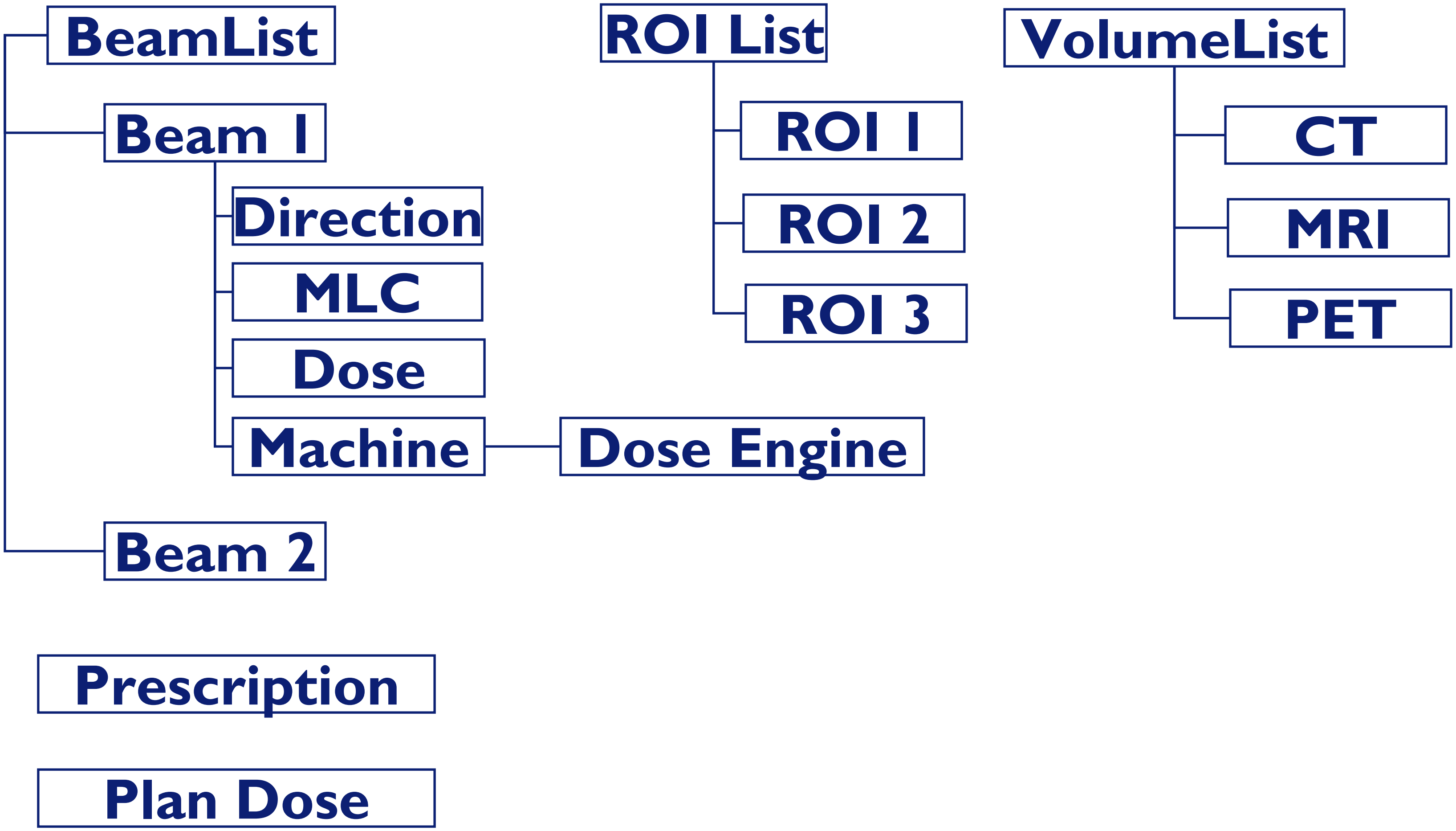
Model

Pinnacle Process: beams, dose engines, etc.

Query Messages

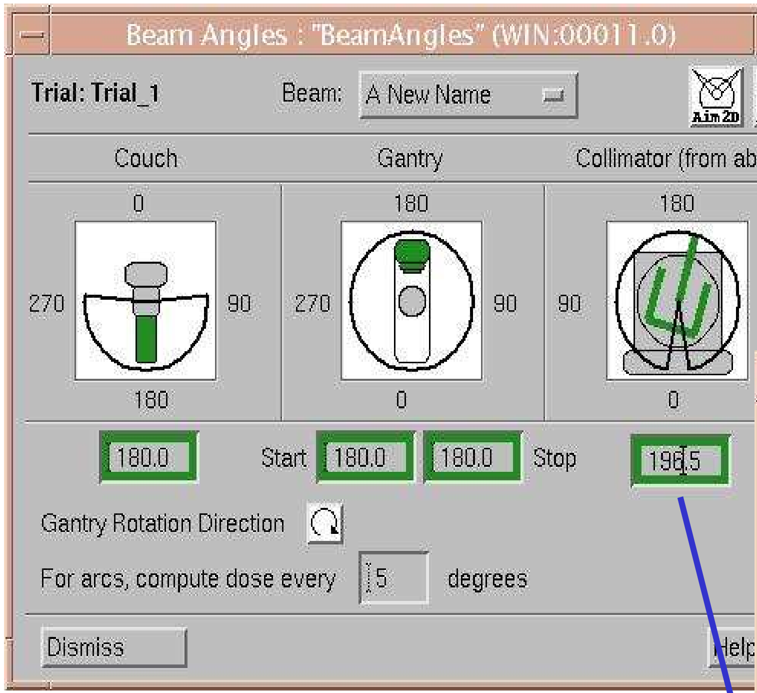
Set or Action Messages

Treatment Planning Components



User Interface View/Controller

TrialList.Current.BeamList.Current.Collimator



Beam Angles : "BeamAngles" (WIN:00011.0)

Trial: Trial_1

Beam: A New Name

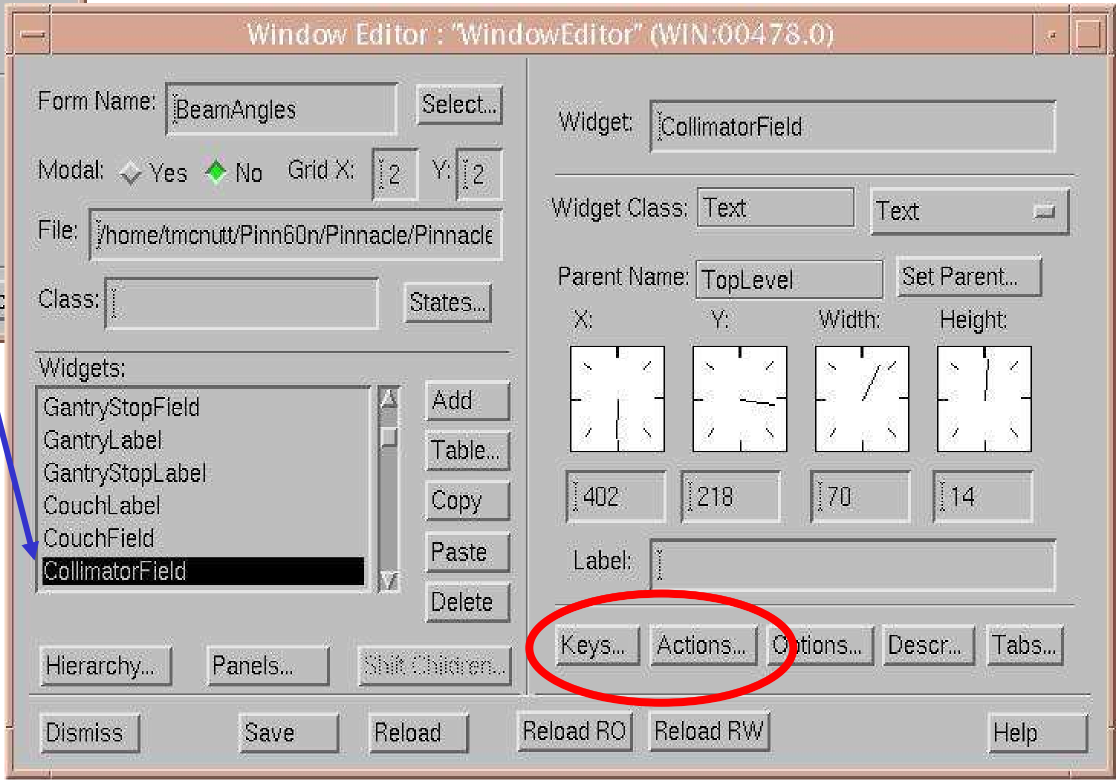
Couch: 180.0

Start 180.0 180.0 Stop 196.5

Gantry Rotation Direction

For arcs, compute dose every 5 degrees

Each widget in the UI is used to both "view" and "control" the Pinnacle "model"



Window Editor : "WindowEditor" (WIN:00478.0)

Form Name: BeamAngles

Modal: ○ Yes ● No Grid X: 2 Y: 2

File: /home/tmcnutt/Pinn60n/Pinnacle/Pinnacle

Class:

Widgets:

- GantryStopField
- GantryLabel
- GantryStopLabel
- CouchLabel
- CouchField
- CollimatorField

Widget: CollimatorField

Widget Class: Text Text

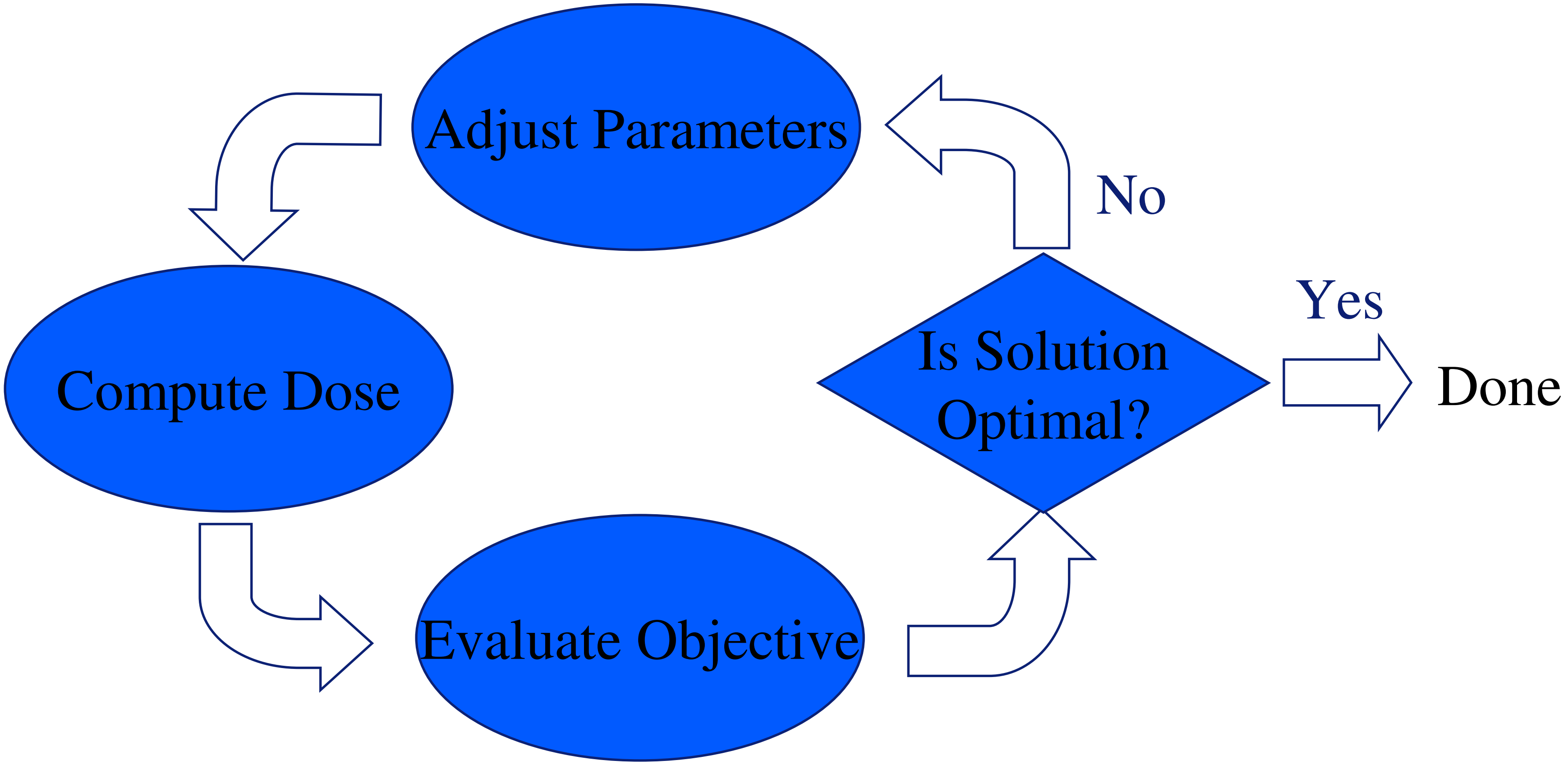
Parent Name: TopLevel

X:	Y:	Width:	Height:
402	218	70	14

Label:

Allows for the UI to be modified without recompiling the source code

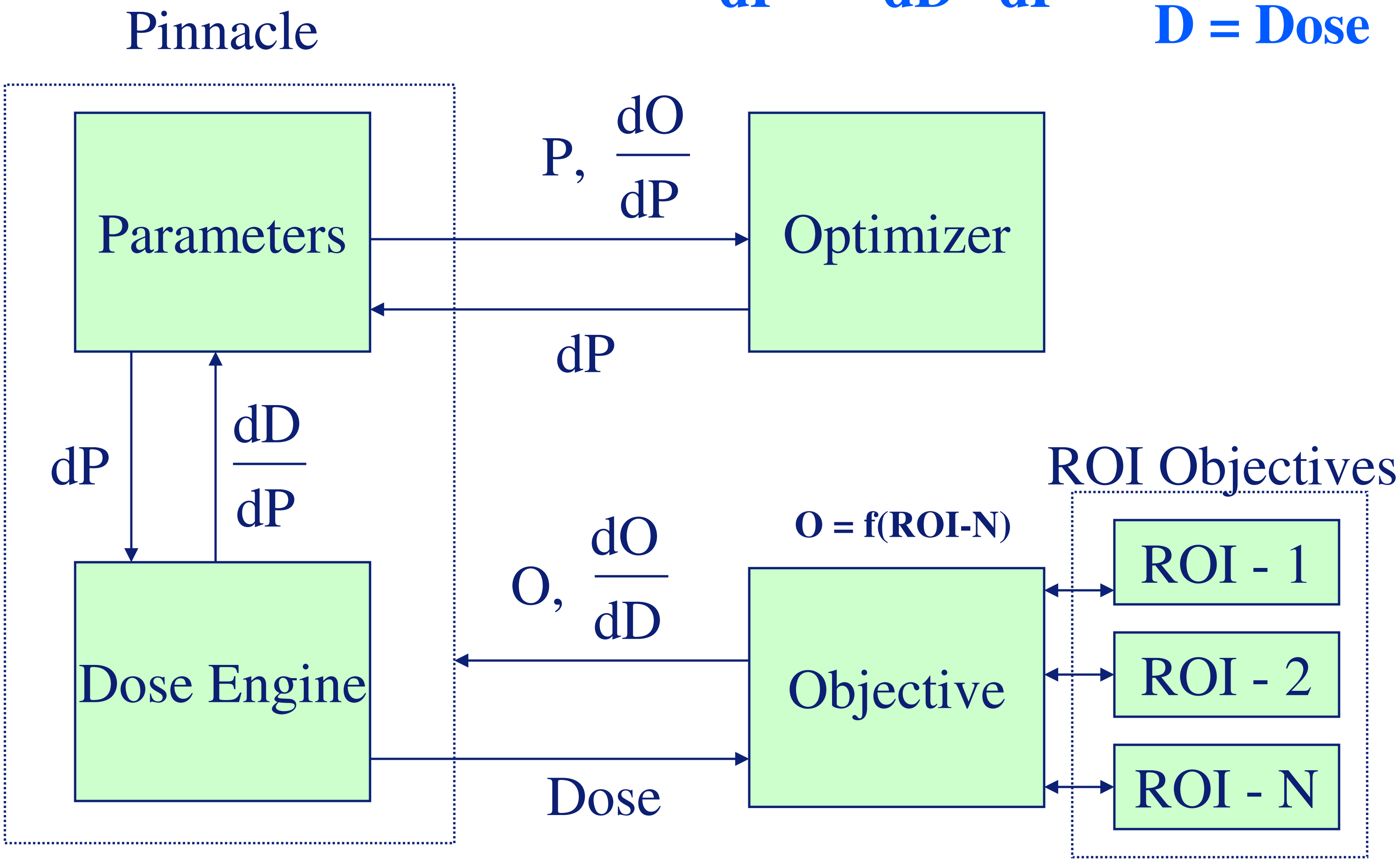
Iterative Optimization



Modular Architecture

$$\frac{dO}{dP} = \frac{dO}{dD} \circ \frac{dD}{dP}$$

O = Objective
P = Parameter
D = Dose

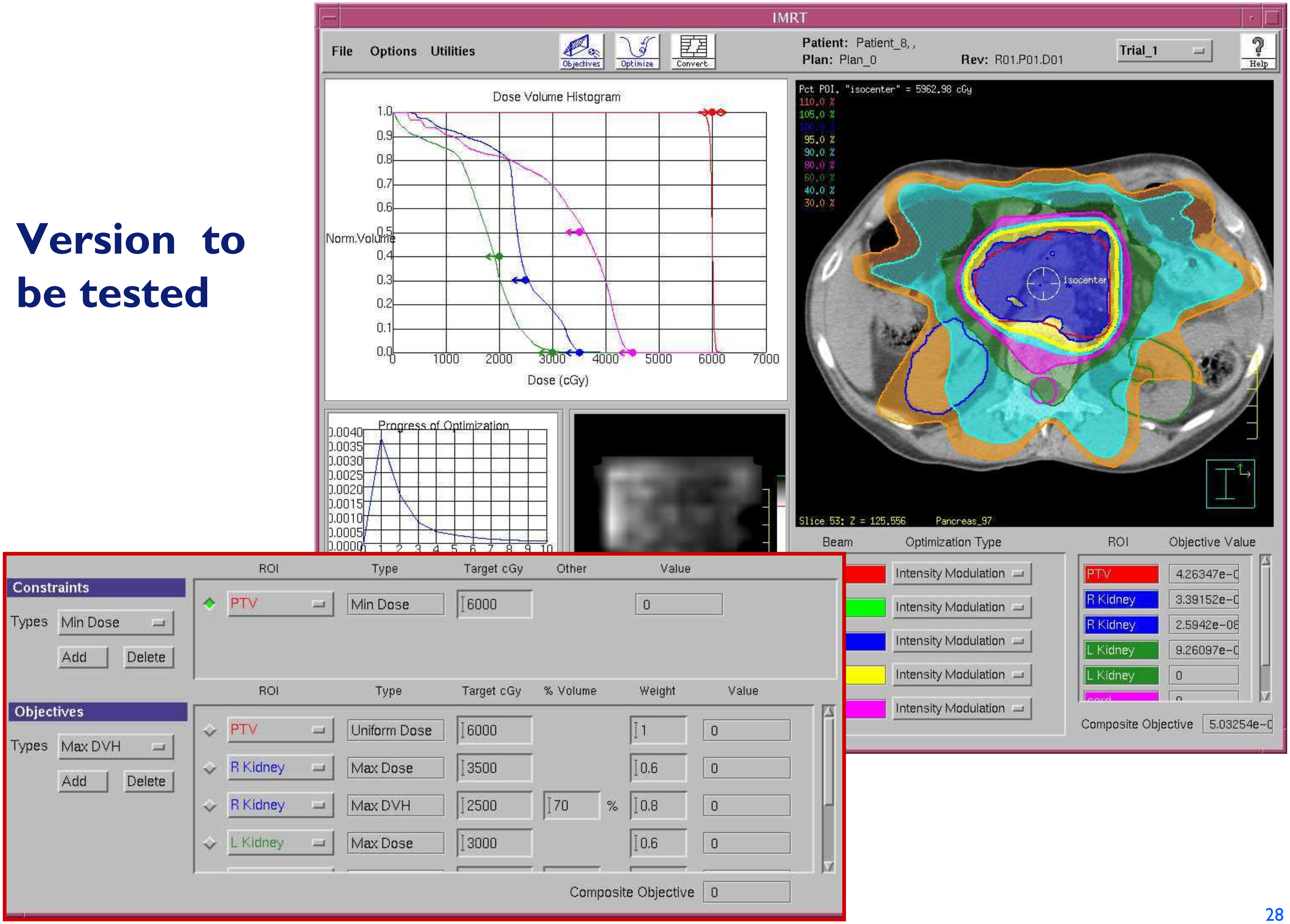


Treatment Parameters and Dose

Want High Speed for Optimization

Parameter	Dose Engine
None	None
Beam Weight	Dose Summation
Segment Weight	Segment Dose Summation
Intensity Modulation (IMRT)	Delta Pixel Beam
Beam Direction	Recompute or interpolate
Aperture Shape / DMPO	Delta Pixel Beam
Wedge Angle	Wedge Summation (Dynamic)
Fractionation Schedule	Re-sum for prescription

Version to be tested



Patient: Patient_8, ,
Plan: Plan_0 **Rev:** R01.P01.D01

Pct POI, "isocenter" = 5962.98 cGy
110.0 %
105.0 %
100.0 %
95.0 %
90.0 %
80.0 %
60.0 %
40.0 %
30.0 %

Slice 53: Z = 125.556 Pancreas_97

Beam	Optimization Type
🟥	Intensity Modulation
🟩	Intensity Modulation
🟦	Intensity Modulation
🟨	Intensity Modulation
🟪	Intensity Modulation

ROI	Objective Value
PTV	4.26347e-0
R Kidney	3.39152e-0
R Kidney	2.5942e-08
L Kidney	9.26097e-0
L Kidney	0
cord	0

Composite Objective 5.03254e-0

Constraints

Types Min Dose

Add Delete

	ROI	Type	Target cGy	Other	Value
◆	PTV	Min Dose	6000		0

Objectives

Types Max DVH

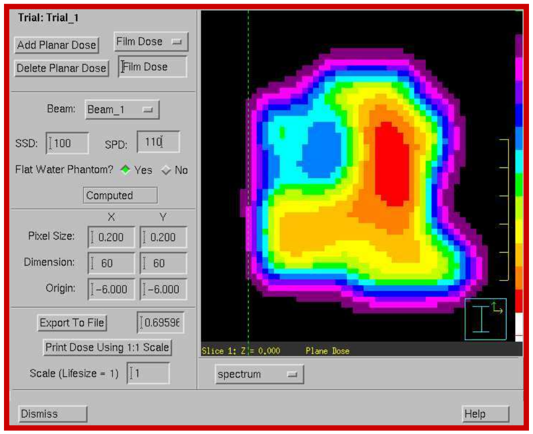
Add Delete

	ROI	Type	Target cGy	% Volume	Weight	Value
◇	PTV	Uniform Dose	6000		1	0
◇	R Kidney	Max Dose	3500		0.6	0
◇	R Kidney	Max DVH	2500	70 %	0.8	0
◇	L Kidney	Max Dose	3000		0.6	0

Composite Objective 0

Validation look at interoperability

- Performance assessment
- Use case verification on patient data
- DICOM RT data transfer
  - RT Plan
  - RT Structure Set
  - RT Image
- Supports linear accelerator
- Dose accuracy compare to measurement



Trial: Trial_1

Film Dose

Film Dose

Beam: Beam_1

SSD: 100 SPD: 110

Flat Water Phantom? ● Yes ○ No

Computed

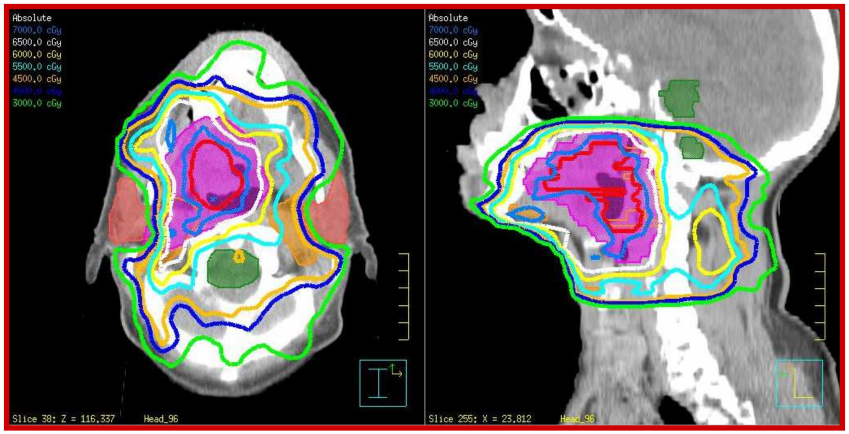
	X	Y
Pixel Size:	0.200	0.200
Dimension:	60	60
Origin:	-6.000	-6.000

0.69596

Scale (Lifesize = 1) 1

Slice 1: Z = 0.000 Plane Dose

spectrum



Happy Developing...

…or Documenting and Testing.