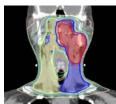
## Automation in Therapy: The Future is Now

## Automated treatment planning



Laurence Court University of Texas MD Anderson Cancer Center Houston TX

lecourt@mdanderson.org



## Conflicts of Interest

- Funded by NCI UH2 CA202665
- Equipment and technical support provided by:
  - Varian Medical Systems
  - Mobius Medical Systems
- $\bullet\,$  Other, not related projects funded by NCI, CPRIT, Varian, Elekta

٠	MD	Anderson	Cancer	Center,	Houst

- · Laurence Court, PhD
- Joy Zhang, PhD algorithms and integration
- Rachel McCarroll H&N algorithms Kelly Kisling, MS – GYN, breast algorithms
- Jinzhong Yang, PhD atlas segmentation Peter Balter, PhD - radiation physics
- Ryan Williamson, MS software tools
- Ann Klopp, MD/PhD GYN planning
   Anuja Jhingram, MD GYN planning
- Simona Shaitemman, MD breast David Followill, PhD audits/deployment
- James Kanke and dosimetry team

Stanford
• Beth Beadle, MD/PhD – head/neck

- Commercial Partners

  Varian Medical Systems

  Mobius Medical Systems

## Primary Global Partners

- · Stellenbosch University, Cape Town
  - Hannah Simonds, MD
  - Monique Du Toit physics
  - Chris Trauernicht physics
  - Vikash Sewram, PhD
- University of Cape Town
  - Hester Berger, PhDDavid Anderson, MD
  - Jeannette Parkes, MD
- · Santo Tomas University, Manila
  - Michael Mejia, MD
  - Maureen Bojador, MS (physics) - Teresa Sy Ortin, MD

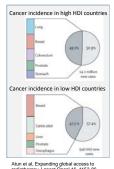
- Global testing sites
- University of the Free State
   William Shaw, PhD
  - Alicia Sherriff, MD

## Cancer across the world

- Low and Middle Income Countries (LMICs)
  - Population: 5.625 billion (84%)
     Global Burden of Disease (97%)

  - 29.4% Communicable diseases 70.6% Non-communicable diseases
  - 66% of global cancer mortality15% of radiation facilities
- Affordable Cancer Techologies (NCI) projects
- <u>Phase 1 (UH2):</u> Development Phase 2 years to April 2018

   System development at MDACC, initial testing at partner sites Phase 2 (UH3): Validation Phase – 3 years
  - · Full patient testing



## Motivation for automated planning 1: Staff shortages

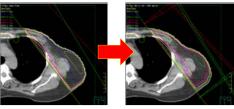
Country	Additional num	ber of radiother	apy infrastructu	re and staffing
	Treatment	Radiation	Medical	Radiation
	units	oncologists	physicists	therapy
				technologists
Philippines	140	141	133	382
South Africa	56	93	82	82
All LMI	9169	12,147	9,915	29,140

Dotto NR, Somiel M, Bodis S. Radiation Therapy infrastructure and Human Resources in Low- and Middle-income Countries: Present Status and Projections for 2020. International Journal of Radiation Oncology\*Biology\*Physics. 2014;88/31/48-52.

- Large deficit in resources including medical physicists and technologists
- Staff retention is also a problem (anecdotal)
- Many international guidelines suggest that medical physicists need 2+ years residency, typically following graduate school so 4+ years per person.
- · Approximately 50% of physicist time is spent doing treatment planning
- $\bullet~$  If planning was automated, then the deficit of medical physicists could be reduced to ~5000.

## Motivation 2: 3D planning

- All our partner institutions are treating chest walls using standard opposed oblique open fields (i.e. not optimized for the individual patient's geometry)
- Automated planning could change this

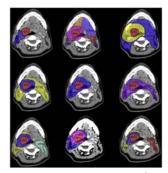


Comparison of the dose distribution for a chest wall treatment with optimized wedges (right) and with open fields (left). The non-optimized plan has a large region of soft tissue receiving 60Gy (6000cGy), compared with 52Gy (5200cGy) in the optimized plan.

## Motivation 3: Consistency

- Head and neck (H&N) tumors are typically surrounded by a large number of OARs
  - CTV delineation a particularly difficult and time consuming task
  - Several reports of high inter-observer variability
  - Automating this process:

    - Reduced contouring time
       Potentially reduce contouring variability



## Specific goals of the Radiotherapy Planning Assistant (RPA)

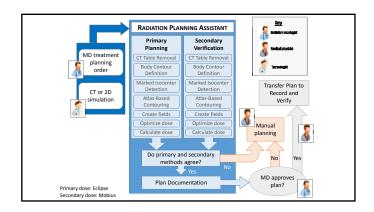
- Automatically create high quality radiation plans for cancers of the:

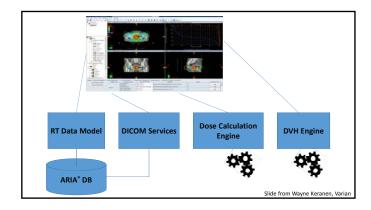
  - Uterine Cervix
     Breast (intact and chest wall)
  - Head and neck (nasopharynx, oropharynx, oral cavity, larynx, etc.)
- Generate treatment plans that are:
  - Generated from scratch (including transfer to the local machine) in less than 30 minutes.
  - Compatible with all treatment units and record-and-verify systems.
     Internally QA'd in an automated fashion within the system.
- Limit need for the radiation oncology physician to:
  - Delineate the target (location).
  - · Provide the radiation prescription.
  - Approve the final plan.
- Create a system that can be used by an individual with:
  - A high school education.

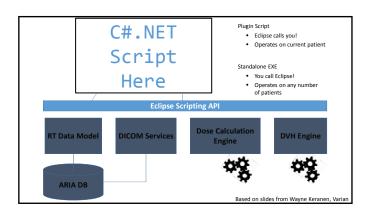
  - ¼ day of training (online and video) on the RPA itself.
     (dosimetrists still needed for unusual/complex cases)

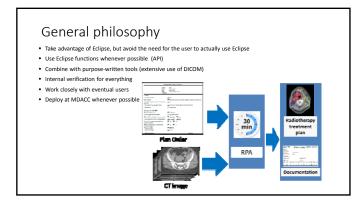
## A comment about Treatment Planning Systems

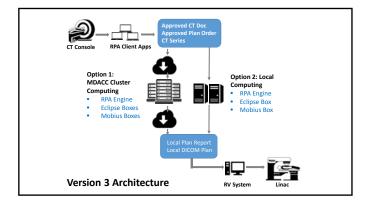
- Our experience is based on the Eclipse TPS
- Similar automation tasks can be achieved with other TPS and I will try to highlight some of these
- Several (TPS agnostic) tools have been deployed into our clinic (Pinnacle and Raystation)



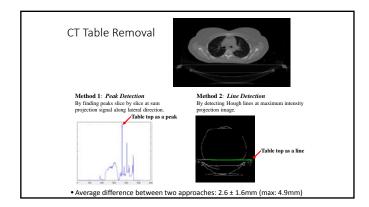


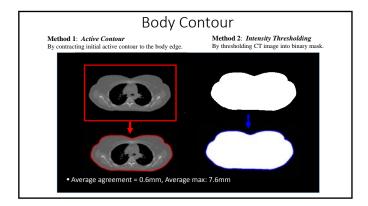


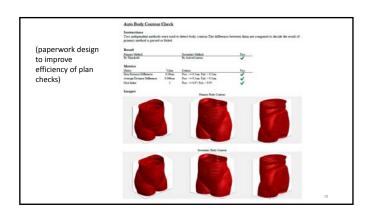


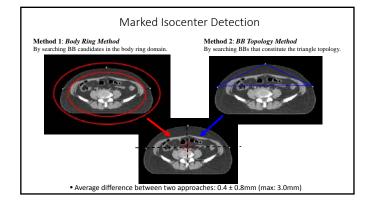


Pre-processing

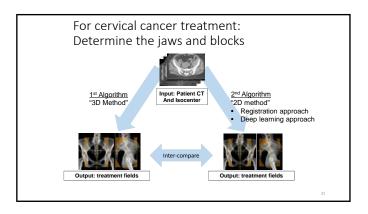


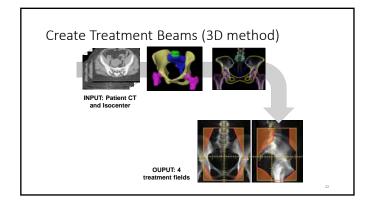


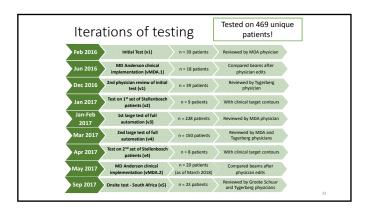


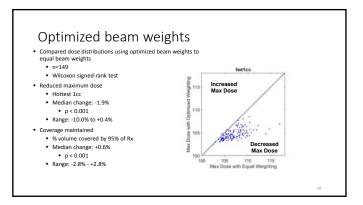


Cervix





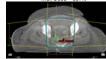




## Greatest effect for hotter doses

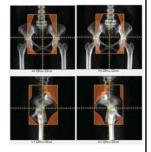
- Looking at patients with higher maximum doses
  - >= 107% of Rx
- Reduced maximum dose
  - Hottest 1cc
  - Median change: -3.5%
- Percent of patients
  - Equal weights: 44% Optimized weights: 3%





## The Big Test

- Retrospective
- MDACC patients (n=150)
- Radiation Oncologist rates fields as acceptable for treatment or not (pass/fail)
   Target pass rate is 95%
- 2 Radiation Oncologists (MDACC and Stellenbosch U)
- Pass rate
- 89% of patients(round 1 = 78%)
- #1 cause of rejection: superior border
  - Otherwise, 99% of plans are acceptable



Clinical Version Deployed at MD Anderson





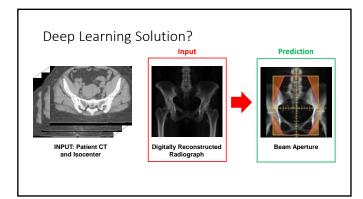
24 patients so far

~10 minutes per patient

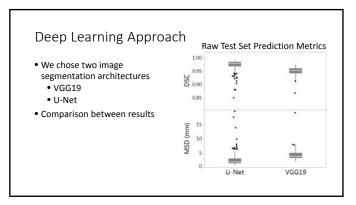
Right Lateral







## Cervical Cancer Beam Aperture Convolutional Neural Networks Local connectivity Provides spatial context Shift invariant Great for Image segmentation VGG-16, U-Net, etc. Image classification AlexNet, VGG, etc. CNNs have become very popular in medical imaging research



Test Set Results Patient # 1 – "Worst" case	
AP PA	RL
U-Net Ground Truth	VGG19

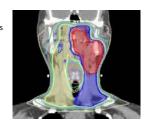
Cervical cancer 4-field box plans - summary	
<ul> <li>Automatic generation of field apertures – used in our clinic</li> <li>Automatic beam-weight optimization</li> <li>Secondary calculations to check quality</li> <li>Currently a complete plan takes ~20 minutes</li> </ul>	

Head and neck

## Head and neck treatments

- Range of complexities in treatments
  - VMAT or IMRT
  - Opposed laterals / off-cord cone-downs
  - Complex conformal plans
- Starting with VMAT (IMRT)
  - Auto-contouring normal tissue
  - Auto-contouring low-risk CTV
     Manual contouring of GTV

  - RapidPlan (Eclipse)



Workflow overview (user's perspective) Radiotherapy treatment plan Physician's Plan Order

Normal tissue contouring

## The search for a good contouring algorithm

Eight Contouring algorithms options evaluated:

- 1. Eclipse Smart Detection (Heuristic)
- 2. Eclipse Smart Segmentation (DIR)
  - a) Single Atlas b) Fused Atlas
- - b) MDACC Atlas
- In-house multi-atlas technique MACS (DIR) [STAPLE fusion]
   MDACC Atlas
   Doriginal Varian Atlas

## Case #3: Normal Tissue Autocontouring

# Results – Physician Review

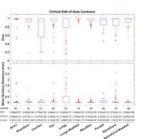
## In-house and commercial solution (RayStation) vs. manual contours

Structures	Co	ommercial solut	tion		In-house solution	on
structures	Dice	MSD (mm)	HD (mm)	Dice	MSD (mm)	HD (mm)
Brain	0.99±0.00	0.8±0.3	16.3±28.3	0.99±0.00	0.8±0.3	16.1±28.5
Brainstem	0.84±0.04	1.8±0.5	6.1±1.9	0.89±0.02	1.4±0.3	6.0±1.9
Spinal Cord	0.85±0.02	1.1±0.2	8.6±3.7	0.84±0.04	1.1±0.2	9.1±4.7
Parotids	0.81±0.05	2.2±0.6	11.8±5.8	0.83±0.05	2.0±0.5	11.9±5.5
Mandible	0.90±0.03	0.9±0.2	8.0±2.8	0.90±0.02	0.9±0.1	7.9±2.6
Cochleae	0.78±0.05	0.7±0.1	2.2±0.5	0.73±0.06	0.8±0.2	2.7±0.4
Eyes	0.88±0.04	1.1±0.3	3.4±0.9	0.89±0.03	1.0±0.2	3.5±0.9
Lungs	0.87±0.11	3.8±3.2	21.5±13.3	0.87±0.12	3.8±3.3	24.3±12.5

Data from Jinzhong Yang and Peter Balter (submitted to ASTRO 2018)

## Clinical use of OAR autocontouring

Analysis of 228 patients (18 months)

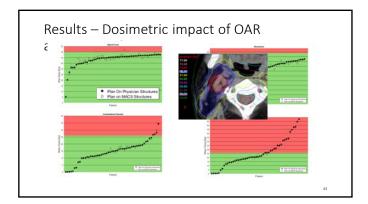


Possible use of margins to account for contouring uncertainties

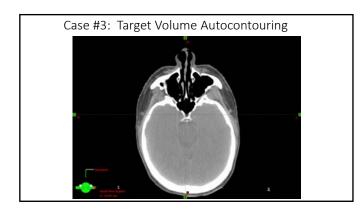
		Patient populat	10n	
		90%	9	5%
		Contour covera	ige	
Structure	95%	100%	95%	100%
Brain	0	7.53	0	10.64
Brainstem	3.55	7.22	4.51	8.88
Cochlea	2.28	3.02	3.42	4
Eye	1.64	3.34	2.06	5.28
Lung	0.64	>15	4.2	>15
Mandible	1.74	12.8	3.59	>15
Parotid gland	4.67	>15	9.05	>15
Spinal cord	0.98	3.74	1.63	4.81

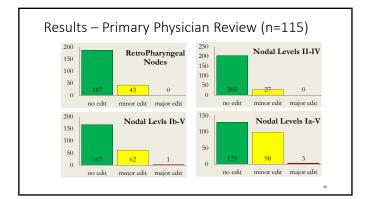
## Dosimetric impact of OAR autocontouring

- 54 patients with clinically edited autocontours
  - Use (1) unedited original and (2) edited contours for planning
     Evaluate the plan on physician edited "true" structures



Target contouring

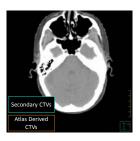




# Results — International Review (5 physicians, n=10) RetroPharyngeal Nodes Nodal Levels II-IV Nodal Levels II-IV

## Deep learning for contour QA?

- Secondary technique
  - Two channel U-Net architecture (3D variant)
    - Trained on 210 bilateral oropharynx patients
  - Requires CT, GTV contour(s), external contour
  - Tested on 85 independent cases: Dice 0.78±0.05



Results – Assessment of autocontour quality	
Nesures Assessment of autocontour quanty	
"Disagreement" with	
secondary check is correlated to disagreement	
with physician CTVs	
0 0.5 1 1.5 2 2.5 Hayasteri Disance - Adas and Physician CTVs	
0	

Plan optimization

Plan automation has been demonstrated to save time:

## Fully Automated Volumetric Modulated Arc Therapy Plan **Generation for Prostate Cancer Patients**

Peter W.J. Voet, RTT, Maarten L.P. Dirkx, PhD, Sebastiaan Breedveld, PhD, Abrahim Al-Mamgani, MD, PhD, Luca Incrocci, MD, PhD, and Ben J.M. Heijmen, PhD

Department of Radiation Oncology, Erasmus MC-Daniel den Hoed Cancer Center, Rotterdam, The Netherlands

Int J Radiation Oncol Biol Phys, Vol. 88, No. 5, pp. 1175-1179, 2014

- Purpose single-run optimization, avoiding manual tweaking
- Commercial TPS linked to in-house optimizer for pre-optimization
- Demonstrated fully automated VMAT planning for prostate plans
- Plans were clinically acceptable and saved 1+ hours of hands on

## Methods – Single optimization treatment plans

- · Planning Approach
  - Physician drawn targets and OARs
  - · Supplement with autocontoured structures
    - · Missing normal structures
    - Various planning structures
  - Isocenter at target center

  - Collimator size/angle based on targets
     30° and 330° collimator angles, symmetric fields, 18cm max
    - 90° collimator angle, split field if Superior-Inferior dimension exceeds 18cm
  - WUSTL Rapid Plan Model + Population Constrain

  - Normalize such that all PTVs receive ≥98% of prescribed dose to 95% volume







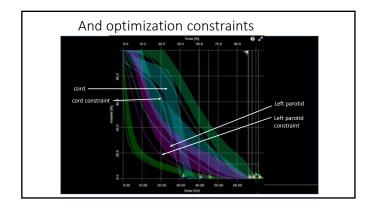


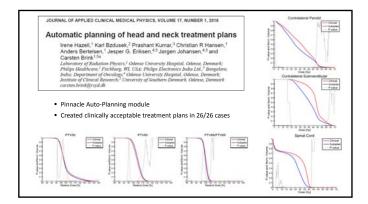


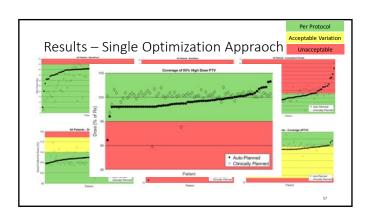


Collimator 30° Collimator 330° X field: 18cm X field: 18cm

## Use Eclipse RapidPlan to predict DVHs



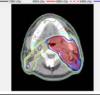




ricsuit	s – c	-111111	cai vs	RPA	piai	15				
		n valu	e. Wilcoxon	Rank Sum	1 1	n valu	e. Wilcoxon I	Rank Sum	% plans	meeting
Structure	Test Point	All (74)			Test Point			MDACC (54)	RPA	Clinical
Spinal Cord	D_max	0.00	0.17	0.00	V_45Gy	0.63	0.25	1.00	100%	99%
Brainstem	D_max	0.00	0.01	0.00	V_50 Gy	1.00	1.00	1.00	100%	99%
Ipsilateral Parotid	D_mean	0.00	0.00	0.10	V_30Gy	0.00	0.00	0.00	56%	50%
Contralateral Parotid	D_mean	0.02	0.00	0.00	V_30Gy	0.01	0.00	0.76	88%	86%
Ipsilateral SMG	D_mean	0.00	0.31	0.01					10%	25%
Contralateral SMG	D_mean	0.00	0.81	0.00					32%	46%
Cochleae	D_max	0.00	0.00	0.00	V_35Gy	0.01	0.25	0.00	86%	93%
Optic Chiasm	D_max	0.02	0.75	0.03	V_54Gy	1.00	1.00	1.00	95%	100%
Optic Nerves	D_max	0.00	1.00	0.00	V_54Gy	0.03	1.00	0.03	90%	96%
Lens	D max	0.00	0.13	0.00	V_7Gy	0.00	1.00	0.00	82%	88%
High Dose PTV	V_1cc	0.00	0.22	0.00					99%	100%
High Dose PTV	V_95%	1.00	1.00	1.00					97%	97%
Intermediate Dose PTV	V_95%	0.00	0.26	0.00					97%	100%
Low Dose PTV	V_95%	0.00	0.02	0.02					100%	100%
		RI	PA plans are I	oetter		Clin	ical plans are	better		

## Head and neck automated planning summary

- Automated contouring of normal tissues deployed into clinic
- Automated contouring of targets works (not deployed)
- Automated VMAT plans
- Currently, the entire automated process takes ~40minutes





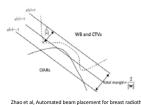


Breast

## Automated breast planning Purdie: Princess Margaret approach Zhao et al: Support vector machine algorithm to determine beam placement Wire placed around the breast tissue or along chest wall Markers used to denote margins (4)

- Heuristic optimization to place beams (based on lung, heart contours)
- Originally integrated into Pinnacle. Now available in RayStation

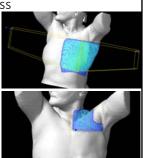




Chest wall – works-in-progress

- Autocontour chest wall, lung, heart, SCV, humeral head, spinal canal, trachea and cricoid
- SVM for gantry, collimator angles, and medial border for SCV field (tangents first, then SCV)
- BEV of cricoid and humeral head for rest
- Field-in-field apertures/weight optimization





Physician feedback



Data gatherir	ig trips, 9/2017, 1/2	018, 3/2018
nto Tomas University, Manila	Tygerberg Hostpital, Stellenbosch University	Groote Schuur Hospital, University of Cape Town
Head/neck treatments	<ul> <li>Cervical cancer treatments</li> </ul>	Cervical cancer treatments
<ul> <li>Reviewed 20 patient RPA plans with radiation oncologist</li> </ul>	<ul> <li>Ran 10 cervical cancer patients through the RPA and reviewed with rad onc (~1hour)</li> </ul>	<ul> <li>Ran 13 cervical cancer patients through the RPA and reviewed 4 rad onc ~1hour</li> </ul>
<ul> <li>They approved all plans</li> </ul>	<ul> <li>She approved all 10 plans</li> </ul>	She approved all 4 plans
<ul> <li>Ran 3 patients through RPA, and reviewed – approved</li> </ul>	Head/neck treatments	Head/neck treatments
Plans for which V105 > 8% are flagged to the user	Ran 5 + 3 H/N patients through the RPA and reviewed with radiation oncologist She approved all plans	Reviewed 3 patient RPA plans with radiation oncologist     They approved all plans
A MARIE SOLVE		

Quality Assurance

## Quality Assurance Basic QA of input data Does the site match? H/N vs. pelvis Is the orientation correct? CT scan length sufficient? Simple image registration Comparison of primary and secondary algorithms algorithms • Dose calculation: Eclipse vs. Mobius • Other independent algorithms for all other functions • Couch removal • Contours • Beam apertures

## **Quality Assurance**

- Comparison with population values
   MU
   Jaw positions
   ........
- Data transfer checks (automatic)
- Manual plan checks
   Planning technician
   Physics
   Radiation oncology

Jaw positions – population statistics

	gantry: 0deg		
	X	у	
average	16.8	21.3	Г
St. dev.	0.9	1.9	Г
min	15.7	18.5	
max	18.2	23.1	Г

Total MU – population statistics

average	208
St. dev.	9
min	200
max	220

	533333333	*****	********	>>>>
	Populate Vide D1 124 D2 11-3 D2 11-3 D3 11-3 D4 11-3 D4 11-3 D4 40 D5 40 D5 40 D6 45 D6 45 D6 45 D7 46 D7 46 D7 46 D7 46 D8 45 D8 5	60, 180, 210 6, 96, 180, 270 8 9 NA, SIA	Provident Value C1.13-4 C0.11-3 C1.13-4 C0.11-3 C0.13-7 C0.10-7 C0.10-7 C1.40-9 C1.4	65, 185 8, 96, 186, 276 8
	Fin Value 13 4.9 30.2 5.7 61.1 34 38.9 38.3 6.21	183 10 8 0 NA 30A	Fin Tibe 63 76 162 87 816 56 287 621	16X 276 8 0
FMILT:	Federal LT Federal S2 (mi) S2 (mi) S2 (mi) S2 (mi) S5D (mi) S6D (mi) S6D (mi) S6D (mi) S6D (mi) S6D (mi) S6D (mi)	Dangy Gusty-Augie Coll: Augie Couch Augie Weige Augia Weige Owen	Field RT Fremete 22 (mil) 22 (mil) 23 (mil) 27 (mil) 27 (mil) 28 (mil) 38 (mil) 38 (mil) 38 (mil)	Davigs Gratey Angle Coll. Angle Couch Engle
	5>>>>>>	*****	היייייי	***
he within population	Process Volse C1.114 C1.114 C1.112 C1.112 C1.112 (C1.112)	6E, 16E, 216 6, 36, 14E, 216 6 5 3A 3A	Population Video (2.1, 12.4) (2.0, 11.2) (2.0, 11.2) (2.0, 11.2) (3.0, 10.1) (3.0, 40.0) (3.1, 40.0) (3.1, 40.0) (3.1, 40.0) (3.1, 40.0)	6C, USS 10, MI, 180, 370 0
reach field should	Fine Value 1.4 4.8 10.2 9.7 80.4 47 11.6 11.7 0.21	UNIX 0 0 0 NA NA	Fire Value 4.3 7.4 10.2 10.2 10.7 10.4 47 10.6 10.0 0.20	1000 1000 0
All parameters for Field AP	To beauty The Topolo beauty Th	Energy Gustry Angle Colf. Angle Creets Angle Wedge Angle Wedge Onest	Field PA Propries XI had XI had YI had YI had YI had HID (no) ME Dupth (no) SE Dupth (no) See Wegte	Emegy Unitty Angle Cell: Angle Creek Angle

## Initial technical review

- Double check of vital plan check functions
- Only get to this point if passes all internal QA checks
- Technical items checked:
  - Marked isocenter
  - Patient orientation, laterality and site
  - Body contour
  - CT processing (couch removal)
  - Field apertures

Library examples

- Any significant artifacts or differences
- Dose calculation complete
- Purpose designed document to lead the user through the checks.



Marked isocenter

Checklist

Uves UNo: Are all 3 fiducials visible on at least one of the slices shown?

Uves UNo: Do the central axis lines touch each fiducial on at least one slice?

Patient results

# Patient results Checklist U'es □No: On the CT slices, is the body correctly contoured (e.g. not including the couch)? U'es □No: Is the body contour smooth, like the library case? U'es □No: Is the orientation consistent with the library case?

## Field apertures Patient Agenture Checklist | Yes | No : Is the patient orientation and body part consistent with the reference case | Yes | No : Are the blocks/MLCs in the acceptable region? | Yes | No : Are there any significant differences between the patient and library images?

Completeness of dose calculation	
BEY+48,8*45% Gy Inodose Ourline Ford AF Ford AF Ford LT	
Check Lise  UNC(DN) is the 69% isotions outline within 2:m of the field appearant.	
Library Case	
	74

How well can the planning technologist evaluate plans?

- Total 7 pages, 23 questions
- Training video (for technical plan checks)
- 4 physics undergraduates, 16 patient plans with intentional errors
- Time taken to check each plan: Average 8 min ?

	Correctly identified errors
Marked isocenter	Yes
Body contour	Yes
Field apertures	NO
Differences in images (including orientation)	Yes
Unanticipated error type (missing field)	NO

Court et al. Radiation Planning Assistant – A streamlined, fully automated radiotherapy treatment planning system, Jove 2018 (accepted)

## Automation of treatment planning: Summary

- Automatic treatment planning may help reduce the planning burden, reducing staff shortages
- Fully automated cervical cancer 4-field box treatments done (20min per plan)
- Field aperture task already at MDA
- Fully automated H/N IMRT/VMAT treatment planning mostly done (40min per plan)
   Normal tissue contouring task deployed at MDA
- Breast / chest wall next
- Start deploying (if funded) late 2018.



lecourt@mdanderson.org