Translating Recent Advances in CBCT to Clinical Practice

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Conflict of Interest

- Co-Investigator: Automatic Organ Segmentation Tool for Radiation Treatment Planning of Cancers. Funded by National Cancer Institute. (R44CA254844)
- No other financial COI to disclose

CBCT for IGRT

- 2002-Flat panel CBCT
- 2003-The concept of “Image guidance for RT”—TR Mackie
- 2006-“Image-guided radiotherapy” –LA Dawson
- Mayo Definition: High-quality images before each treatment session, for accurate and precise delivery of the intended RT

Patient Care & Health Information › Tests & Procedures

Image-guided radiation therapy (IGRT)

www.redjournal.org › article › abstract

Flat-panel cone-beam computed tomography for image ...

David A **Jaffray**, Ph.D. **David** A ... **Cone-beam CT** imaging involves acquiring multiple kV radiographs as the gantry rotates through 360° of rotation. A filtered ...

by DA Jaffray · 2002 · Cited by 1498 · Related articles

www.redjournal.org › article › fulltext

Image guidance for precise conformal radiotherapy ...

Image-guided precision conformal therapy here means the continuous quality improvement using images to better achieve the goals of **radiation therapy**, which is ...

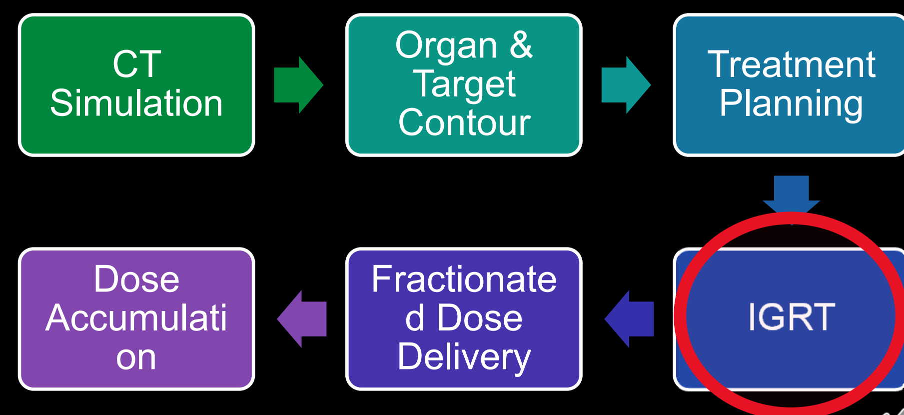
by TR Mackie · 2003 · Cited by 610 · Related articles

pubmed.ncbi.nlm.nih.gov › ...

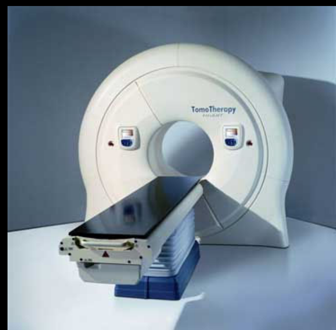
Image-guided radiotherapy: rationale, benefits, and limitations

2006 Oct;7(10):848-58. doi: 10.1016/S1470-2045(06)70904-4. Authors. Laura A **Dawson** ...

by LA Dawson · 2006 · Cited by 332 · Related articles



2000s



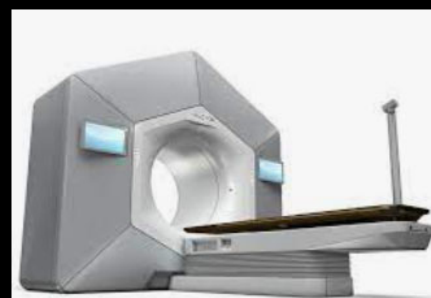
Tomotherapy

C-Arm Linac

Cyberknife

2010s

MRgRT

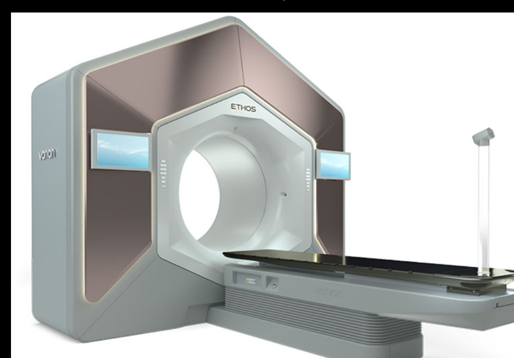


Halcyon

GammaKnife Icon

2020s

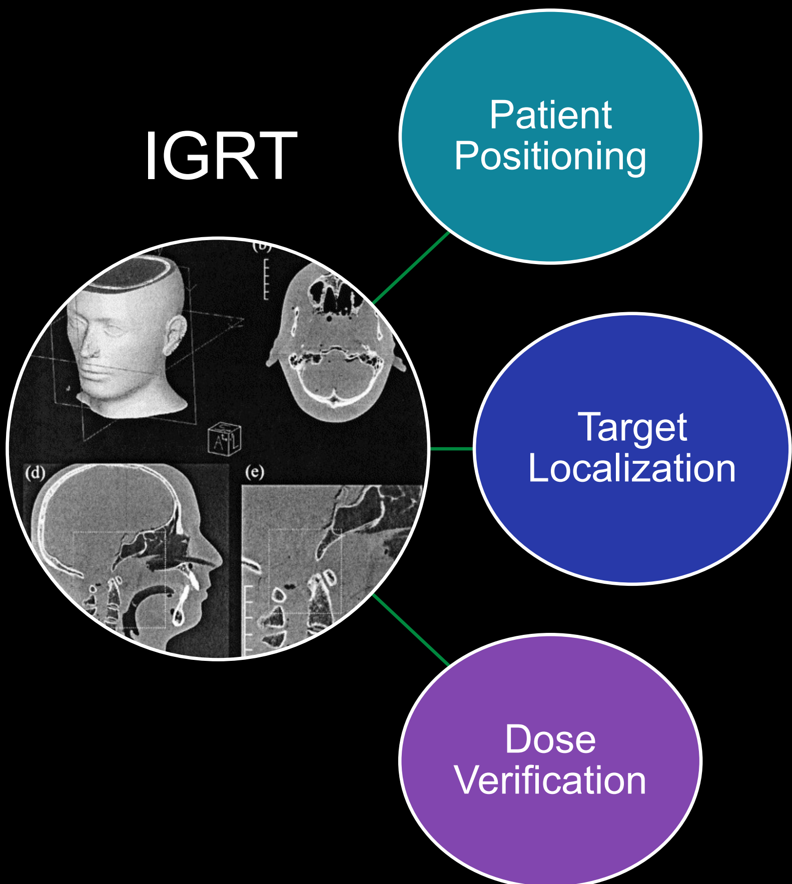
FLASH



Ethos: AI-driven

PET-Linac

CBCT in RT for the past 20 years



- CBCT has been routinely used for IGRT for the past 20 years knowing that:

  -- Inferior image quality compared to CT

  -- Sufficient for IGRT purpose

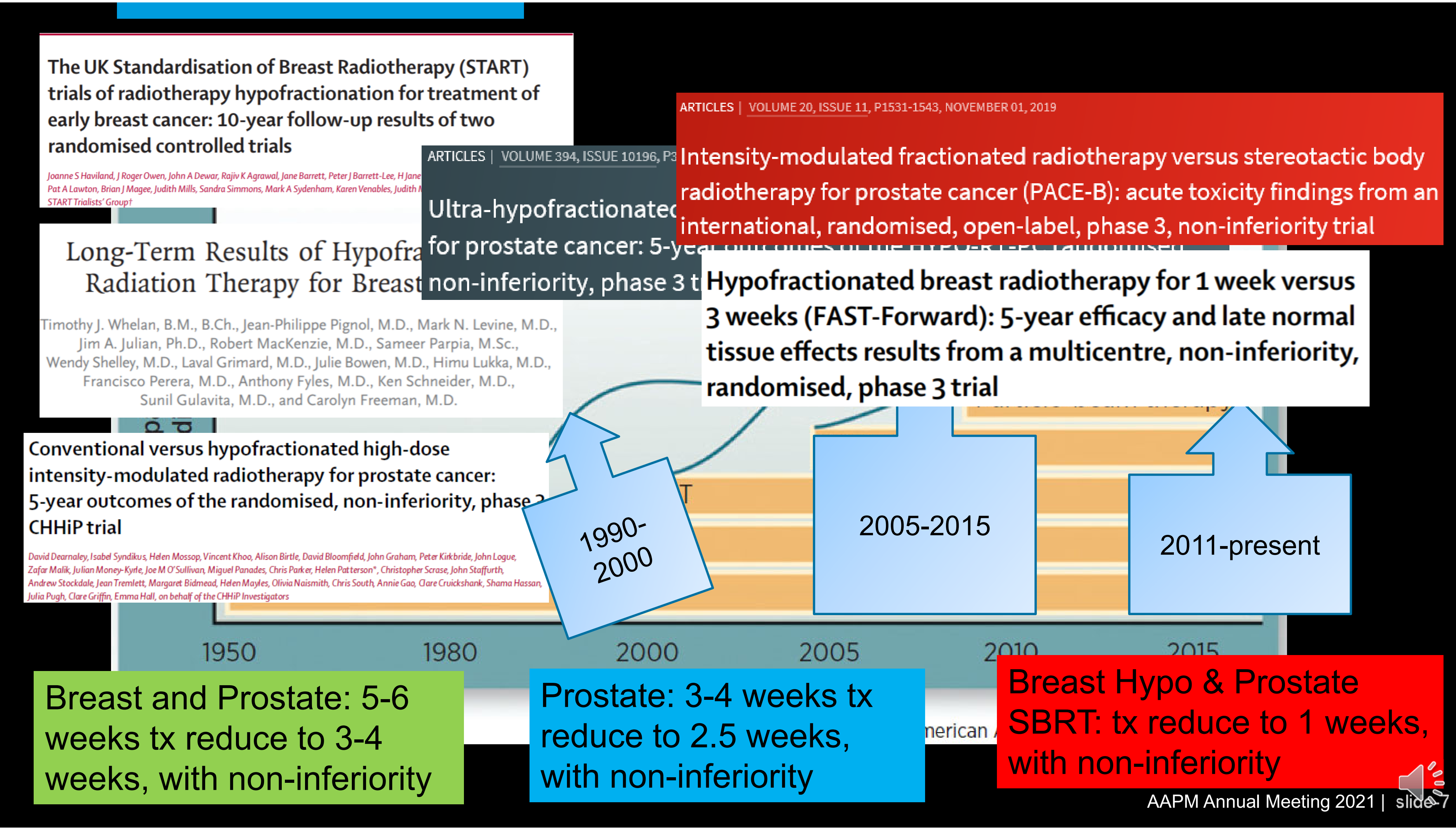
- A paradigm shift in RT:

  -- From conventional fractionation to hypo-fractionation or SBRT

  -- Timescale for treatment is going from weeks to days or even mins

Three Driving Factors for Paradigm Shift

- The field of radiation oncology is driven by quality (clinical outcome and efficacy), efficiency (without sacrificing the outcome), and cost (reimbursement pattern)
  - New commercial products from Vendors;
  - Radiation Oncology Alternative Payment Model
  - What about patient treatment quality?
- Clinical Trials are driving the field towards Hypo-Fractionation and SBRT
  - Traditional SBRT sites: lung, liver, pancreas, and adrenal
  - New sites for hypo-fractionation: Breast and Prostate



The UK Standardisation of Breast Radiotherapy (START) trials of radiotherapy hypofractionation for treatment of early breast cancer: 10-year follow-up results of two randomised controlled trials
Joanne S Haviland, J Roger Owen, John A Dewar, Rajiv K Agrawal, Jane Barrett, Peter J Barrett-Lee, H Jane
Pat A Lawton, Brian J Magee, Judith Mills, Sandra Simmons, Mark A Sydenham, Karen Venables, Judith
START Trialists' Group†
Long-Term Results of Hypofra
Radiation Therapy for Breast
Timothy J. Whelan, B.M., B.Ch., Jean-Philippe Pignol, M.D., Mark N. Levine, M.D., Jim A. Julian, Ph.D., Robert MacKenzie, M.D., Sameer Parpia, M.Sc., Wendy Shelley, M.D., Laval Grimard, M.D., Julie Bowen, M.D., Himu Lukka, M.D., Francisco Perera, M.D., Anthony Fyles, M.D., Ken Schneider, M.D., Sunil Gulavita, M.D., and Carolyn Freeman, M.D.
ARTICLES | VOLUME 394, ISSUE 10196, P3
Ultra-hypofractionate
for prostate cancer: 5-yea
non-inferiority, phase 3 t
ARTICLES | VOLUME 20, ISSUE 11, P1531-1543, NOVEMBER 01, 2019
Intensity-modulated fractionated radiotherapy versus stereotactic body radiotherapy for prostate cancer (PACE-B): acute toxicity findings from an international, randomised, open-label, phase 3, non-inferiority trial
Hypofractionated breast radiotherapy for 1 week versus 3 weeks (FAST-Forward): 5-year efficacy and late normal tissue effects results from a multicentre, non-inferiority, randomised, phase 3 trial
Conventional versus hypofractionated high-dose intensity-modulated radiotherapy for prostate cancer: 5-year outcomes of the randomised, non-inferiority, phase
CHHiP trial
David Dearnaley, Isabel Syndikus, Helen Mossop, Vincent Khoo, Alison Birtle, David Bloomfield, John Graham, Peter Kirkbride, John Logue, Zafar Malik, Julian Money-Kyrle, Joe M O'Sullivan, Miguel Panades, Chris Parker, Helen Patterson*, Christopher Scrase, John Staffurth, Andrew Stockdale, Jean Tremlett, Margaret Bidmead, Helen Mayles, Olivia Naismith, Chris South, Annie Gao, Clare Cruickshank, Shama Hassan, Julia Pugh, Clare Griffin, Emma Hall, on behalf of the CHHiP Investigators
1990-2000
2005-2015
2011-present
1950
1980
2000
2005
2010
2015
Breast and Prostate: 5-6 weeks tx reduce to 3-4 weeks, with non-inferiority
Prostate: 3-4 weeks tx reduce to 2.5 weeks, with non-inferiority
Breast Hypo & Prostate SBRT: tx reduce to 1 weeks, with non-inferiority
AAPM Annual Meeting 2021 | slide 7

Prostate SBRT with online MRgART

Int J Radiat Oncol Biol Phys. 2019 Dec 1;105(5):1086-1094. doi: 10.1016/j.ijrobp.2019.08.007. Epub 2019 Aug 13.

A Prospective Single-Arm Phase 2 Study of Stereotactic Magnetic Resonance Guided Adaptive Radiation Therapy for Prostate Cancer: Early Toxicity Results.

- 101 intermediate-high risk (T1-3bN0M0) prostate cancer patients
- 5 fractions of 7.25 Gy to the target volume using MRgRT daily plan adaptation with simultaneous relative sparing of the urethra to a dose of 6.5 Gy per fraction
- Low incidence of early GI and GU toxicity, both in clinician- and patient-reported outcome measurements

Pancreatic SBRT with online MRgART

Cancer Med. 2019 May; 8(5): 2123–2132. PMCID: PMC6536981
Published online 2019 Apr 1. PMID: 30932367
doi: 10.1002/cam4.2100

Using adaptive magnetic resonance image-guided radiation therapy for treatment of inoperable pancreatic cancer

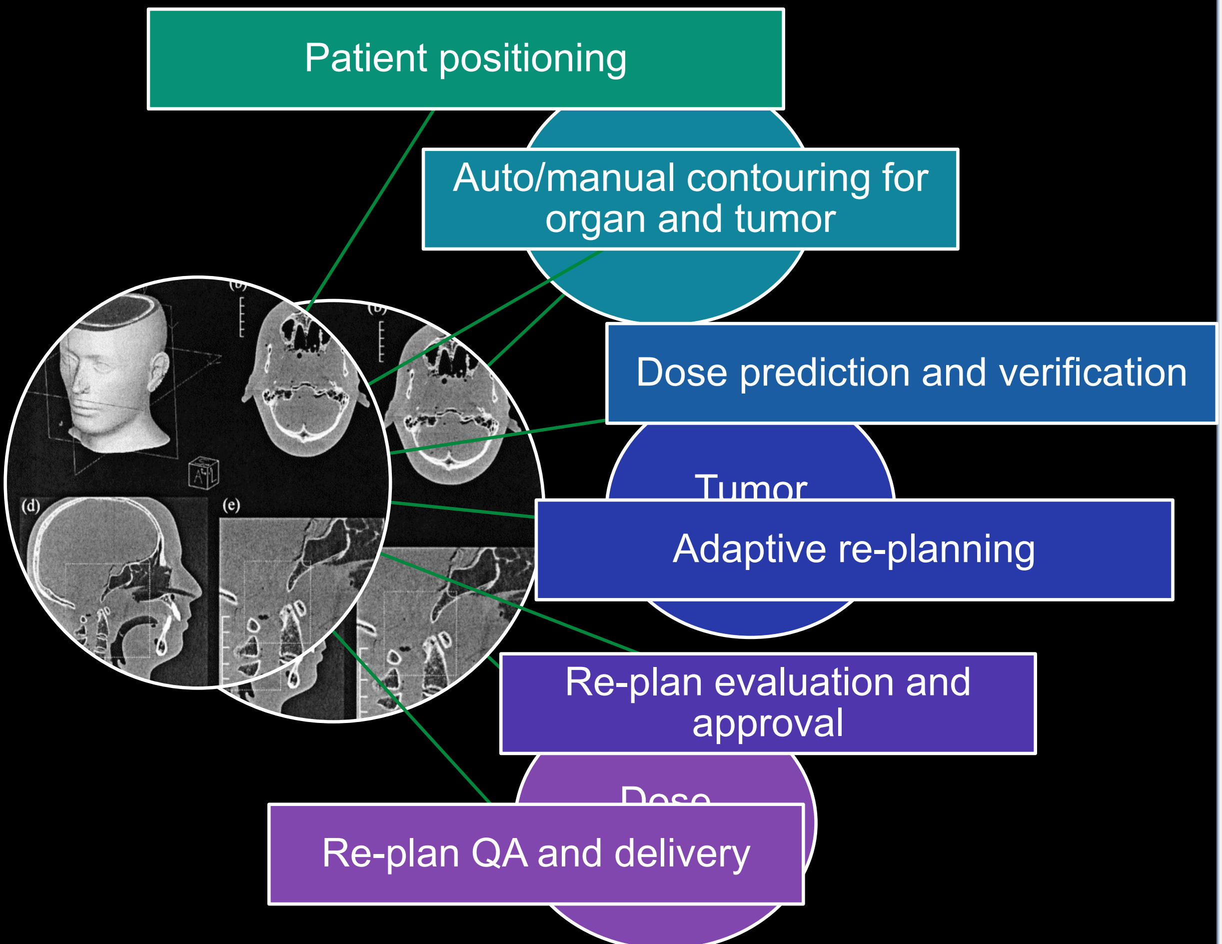
RT technique	Prescription dose & fractionation	Number of patients	Median BED_{10}[range]
Conventionally fractionated	40-55 Gy in 25-28 fractions	13	55.5 [38.2-67.1]
Conventional SBRT	30-35 Gy in 5 fractions	6	55.8 [48.0-59.5]
High-dose SBRT	40-52 Gy in 5 fractions	16	77.6 [72.0-106.1]
Hypofractionated	50-67.5 Gy in 10-15 fractions	9	82.7 [67.8-97.9]

- Five institutions, retrospective review of 44 patients with inoperable pancreatic cancer treated with MRgRT
- Stratified into high-dose ([BED_{10}] >70, n=24) and standard-dose groups (BED_{10} ≤70, n=20).
- Significant improvement in 2-year OS for high-dose patients (49% vs 30%, *P* = 0.03)
- Grade 3+ GI toxicity: 3 for standard-dose and 0 for high-dose group
- Stereotactic MRI-guided On-table Adaptive Radiation Therapy (SMART) for Locally Advanced Pancreatic Cancer (sponsored by ViewRay)

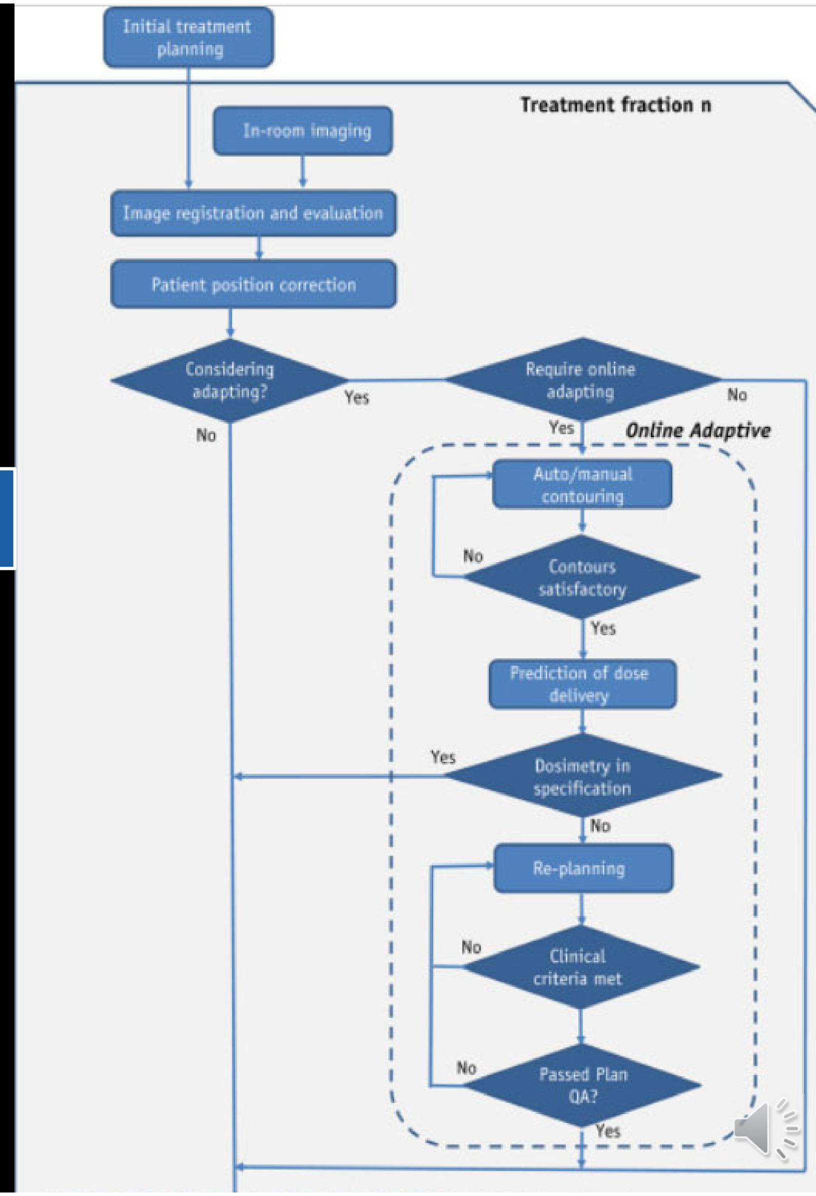
ClinicalTrials.gov Identifier: NCT03621644

Improve daily CBCT image quality for integrated online adaptive radiotherapy: online CTgART

CBCT based Online CTgART



Glide-Hurst, et al. IJROBP, Vol. 109, No. 4, pp. 1054-1075, 2021



Minimum requirements for ART workflow

-- Imaging: HU accuracy (10%), Geometric integrity (1mm), Low contrast resolution, FOV, Artifacts

-- Registration: Deformable image registration and Contour propagation (Dice>0.8)

-- End-to-end: 5% dosimetric accuracy

Table 3 Summary of minimum requirements to consider for ART workflow components

ART component	Element	Suggested minimum requirement	Potential clinical impact
Imaging	HU accuracy	CT number accuracy within 10%	20% variation in HU value may result in a systematic dose error of 1.5%[94]
	Geometric integrity	≤1 mm (within 10 cm radial distance of isocenter)	Inaccurate localization of organs
		≤2 mm (>10 cm radial distance away from isocenter)[95]	Inaccuracies in dose calculation
	Low contrast resolution	Per AAPM TG recommendations for the ART planning modality	Limited boundary detection that may adversely affect accurate delineation
	Consistent physiological state as reference data set (breath-hold/internal filling)	Motion managed within TG-76 recommendations (<5 mm)[96]	Over-/underestimate of target/OAR doses Incorrect state of internal anatomy for treatment planning
	FOV	Contains all relevant anatomy and full integrity skin contour	Inaccurate dose calculation for missing anatomy Lack of one-to-one correspondence may lead to erroneous deformable image registration
	Artifacts	ART planning image shall be free of artifacts in the clinically usable FOV	May obscure relevant anatomy Delineation accuracy adversely affected Dose calculation may be adversely affected
Image registration	Deformable registration	Visual assessment Point-wise registration error or mean distance to agreement within magnitude of maximum voxel dimension[39]	Erroneous deformations may warp images, leading to inaccurate geometry and underlying electron densities
	Contour propagation	Visual assessment Dice similarity coefficient >0.8[39]	Inaccurate dose evaluation due to incorrect target volumes Under- or overestimated volumes
End-to-end/workflow	Localization using	Data integrity verified via TG-53[97]	Localization uncertainties
		f external laser	Input/output discrepancies
		arks:	Systematic offsets introduced
		n	
		nm	
		d dose[5]	Inaccurate dose evaluation

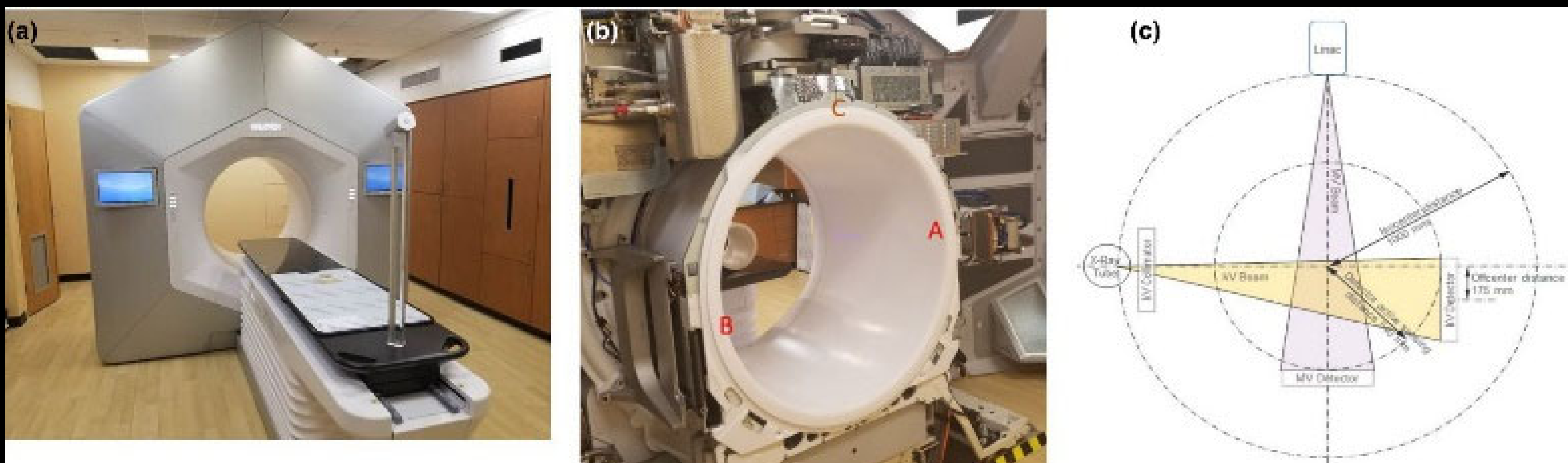
Abbreviations: ART = adaptive radiation therapy; CT = computed tomography; FOV = field of view; HU = Hounsfield unit; OAR = organ at risk.

Does CBCT meet these requirements?
No for FDK_CBCT, but…

Glide-Hurst, et al. IJROBP, Vol. 109, No. 4, pp. 1054-1075, 2021

Improved CBCT on Halcyon Systems

- ✓ Fast gantry rotation: fixed kV geometry and compact design allows the system to achieve a maximum speed of 4 rotations per minute (4 times faster)
- ✓ Scatter reduction: an anti-scatter grid with a high grid ratio of 15:1
- ✓ Advanced reconstruction: iCBCT (Acuros CTS based Iterative recon algorithm)



Halcyon system with a large bore size of 1 m diameter

A: fixed kV source; B: kV detector, and C: MV beamline

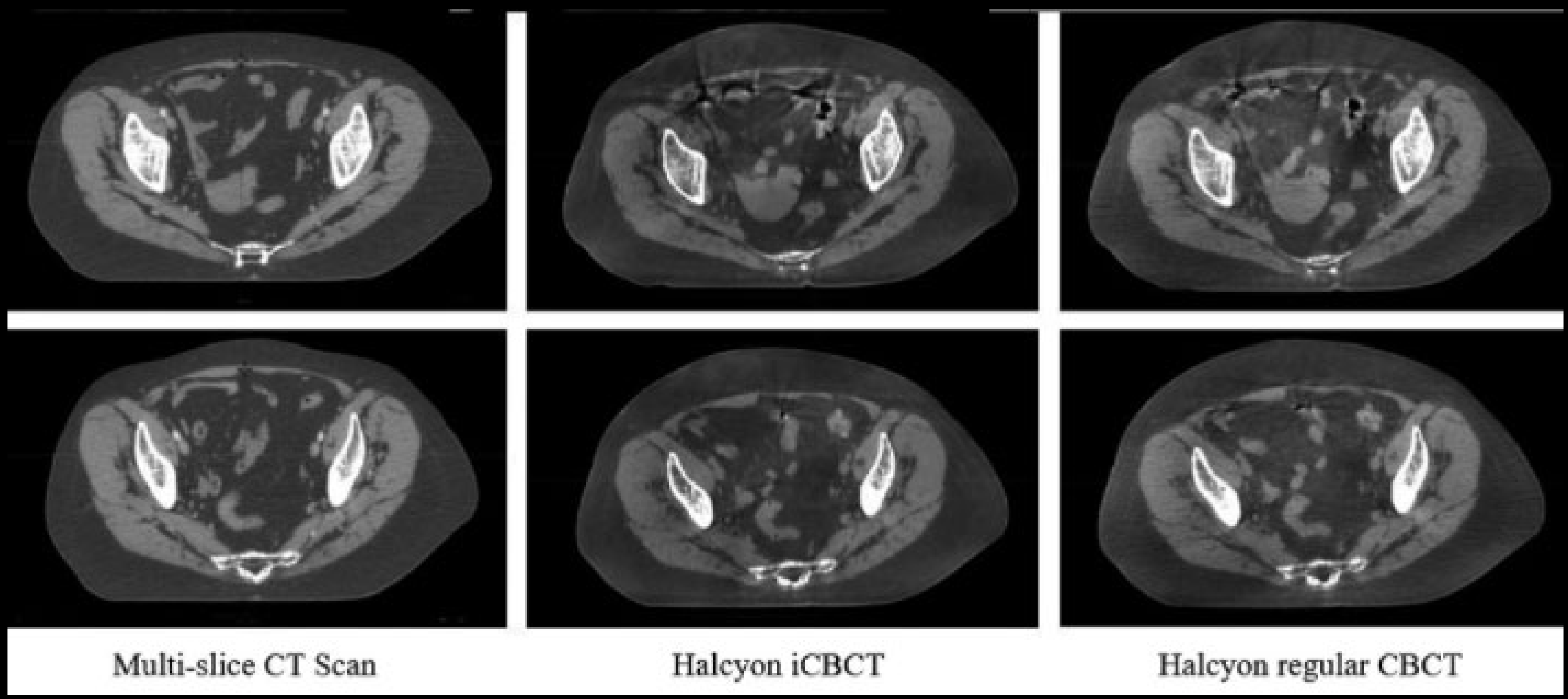
Schematic drawing of the kV and MV beam line

Cai et al. Medical Physics, 46(3), 1355-1370

Acuros CTS-based iCBCT

Iterative CBCT
Adam Wang, PhD Stanford University

- Acuros iCBCT: efficient scatter correction using Acuros CTS and statistical iterative reconstruction, reduce image noise in the second pass of reconstruction while preserving the organ edges
  Wang et al. Medical Physics, 45 (5): 1914-1925

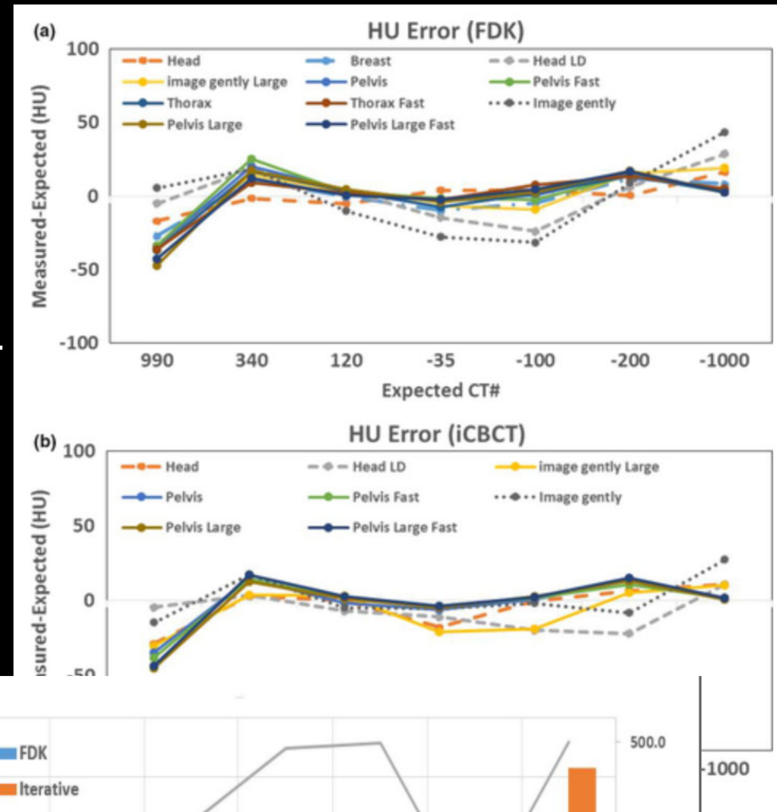


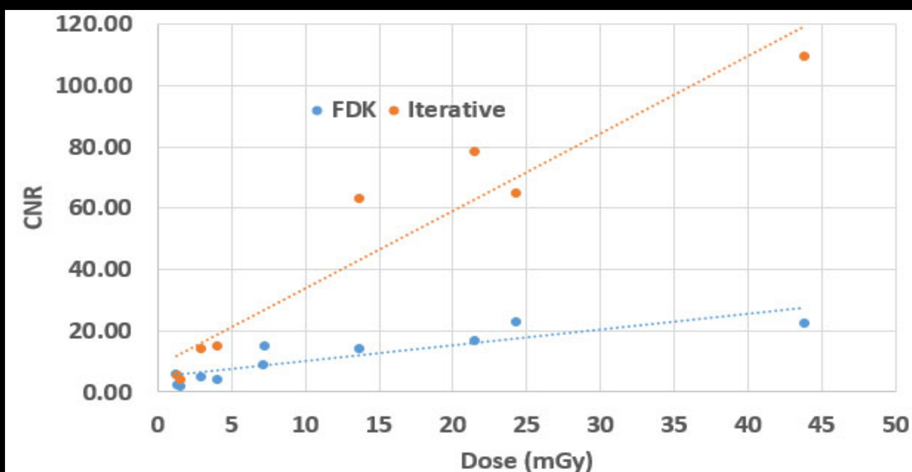
Cai, et al. Medical Physics 46 (3), 2019.

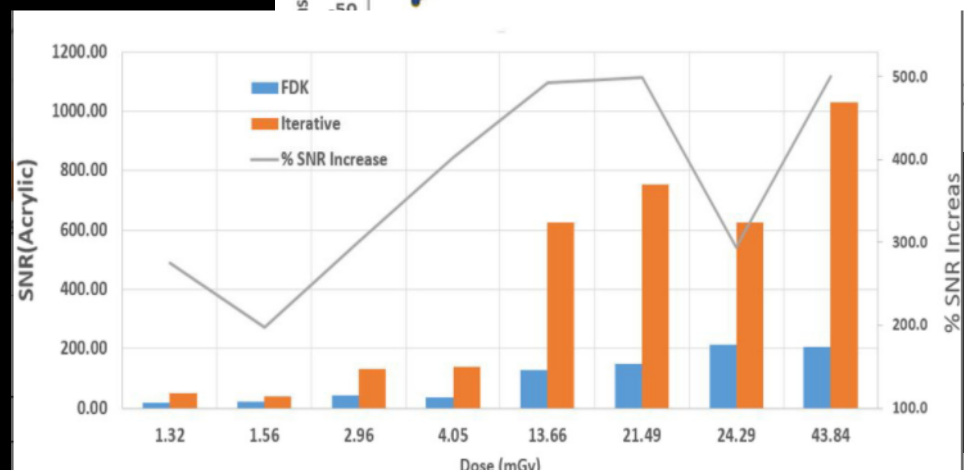
Halcyon iCBCT

Cai, et al. Med. Phys. 46 (3), 2019.

- **Additional recon time:** compared to FDK_CBCT, 10-30s increase, depending on imaging modes
- **HU accuracy:** < 50 HU, comparable to FDK_CBCT
- **CNR and SNR:** SNR on iCBCT-based images increases about 200–500% compared to the FDK-based images yielding the same imaging dose







Halcyon CBCT for online CTgART

- ✓Mechanical accuracy
- ✓Geometric accuracy
- ✓Image registration
- ✓Image contrast
- ✓HU accuracy
- ✓Dosimetric validation < 5%

Cai, et al. Medical Physics 46 (3), 2019.
Jarema et al, Physica Medica, 68, 2019

TABLE III. Tests performed to characterize kV-IGRT system and suggested tolerances.

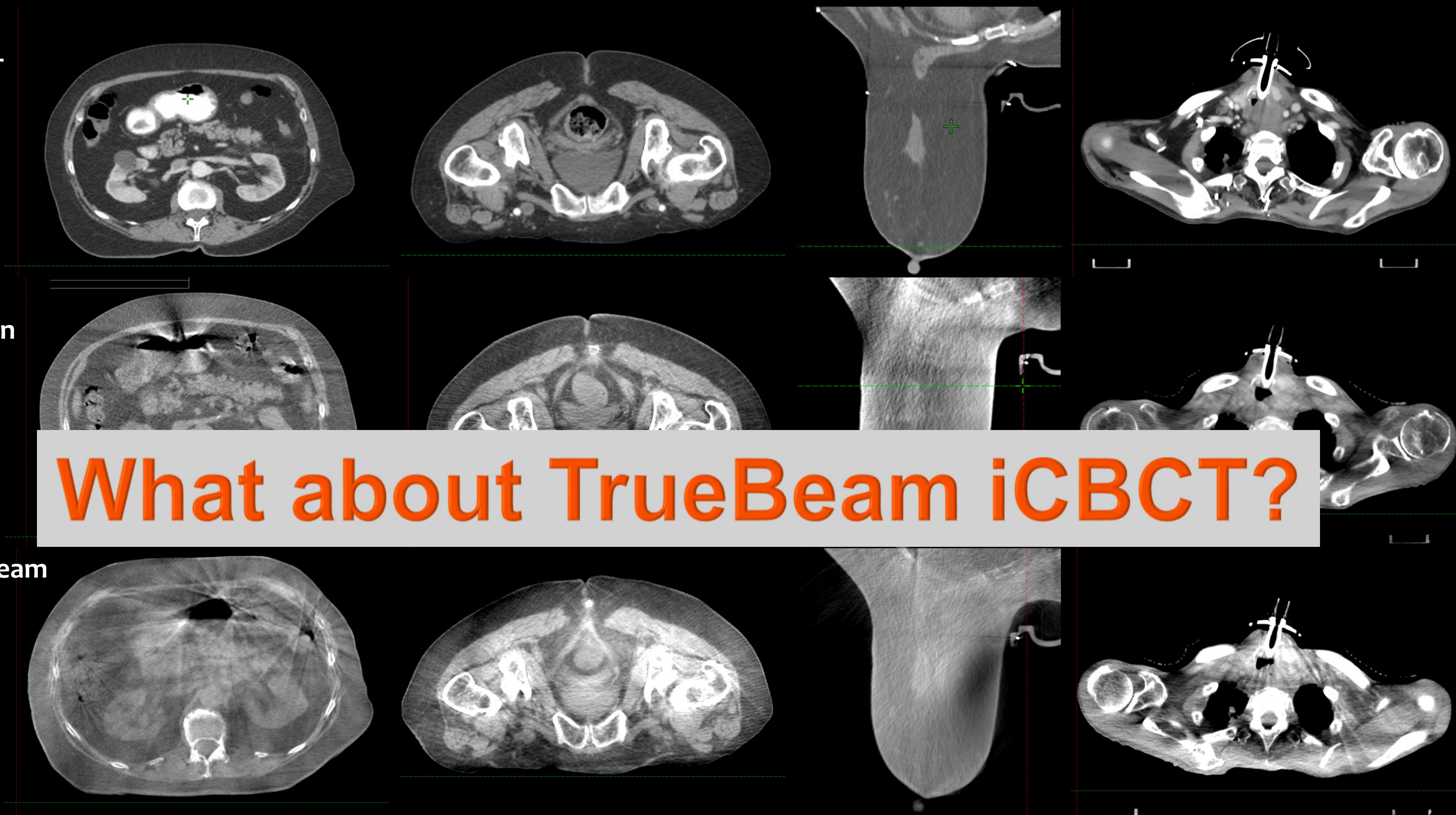
Detailed tests		Test results	Suggested tolerances
Mechanical accuracy	• Laser localization	<1 mm	1 mm
	• kV imager projection offset	<0.2 mm	0.5 mm
	• kV field edge accuracy	<1.7 mm	2 mm
Geometric accuracy	• Imaging and treatment coordinate coincidence	<1 mm	2 mm
Patient setup accuracy	• kV 3D–3D match	<0.5 mm	1 mm
Image quality tests (regular and iCBCT reconstructions on all protocols)	• Spatial resolution	C: ≥5 lp/cm Q: per protocol (0.25–0.68 cycles/mm)	C: not worse than 5 lp/cm Q: per protocol
	• Low-contrast resolution	C: all HU inserts are visible Q: per protocol (2–20 for regular CBCT)	C: all HU inserts are visible Q: >2
	• CT number uniformity	C: ±30 HU Q: ±30 HU	±40 HU
	• CT number consistency	C: ±50 HU Q: ±50 HU	±50 HU
	• Slice thickness	C: <0.5 mm Q: <0.5 mm	0.5 mm
	• Spatial linearity	<1 mm	1 mm
Dosimetry	• kV CBCT dose accuracy	<20 mGy within specs	Per protocol (1–40 mGy)
	• kV CBCT dose consistency	<20 mGy within baseline	Per protocol (1–40 mGy)

Note. In the table, C represents the measurements with the Catphan phantom, and Q represents the measurement with the QUART phantom.

Sim CT

Halcyon CBCT

TrueBeam CBCT

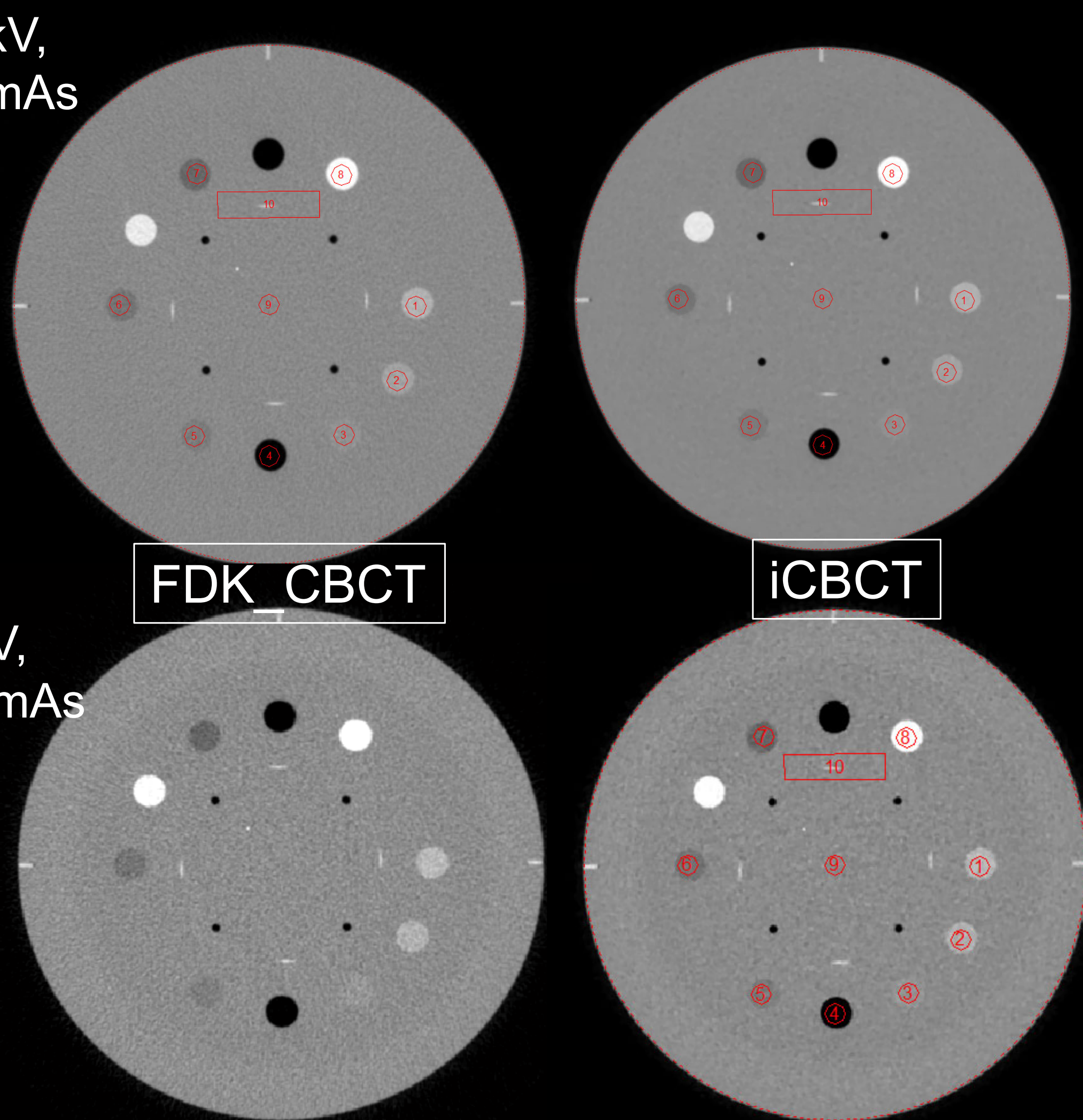


What about TrueBeam iCBCT?

Slide courtesy of Dr. Bin Cai, UT-Southwestern

Cai, et al. Med. Phys. 46 (3), 2019.

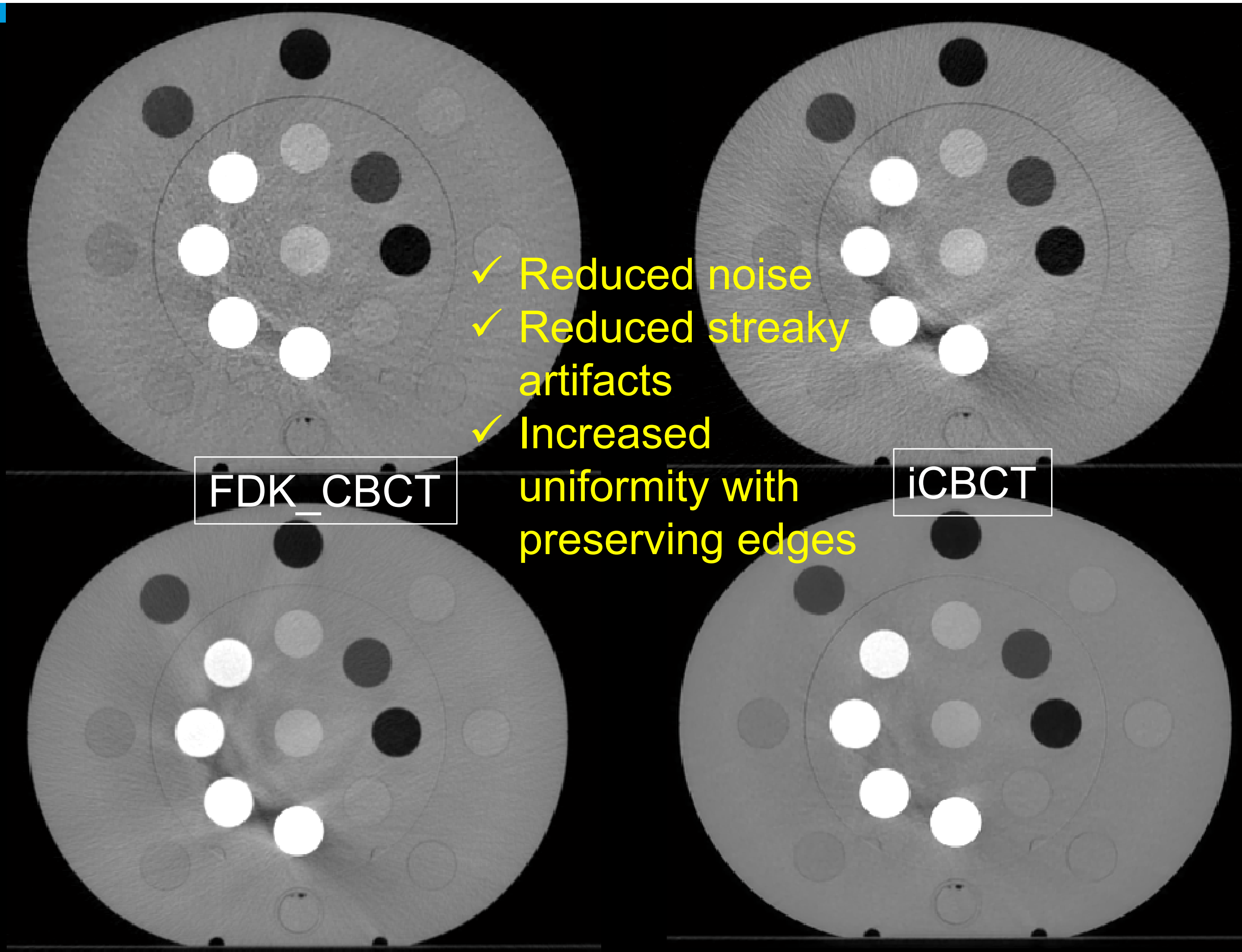
TrueBeam iCBCT



HEAD mode (100kV,150mAs)	FDK	iCBCT
Uniformity	95.8%	98%
Contrast	4.6%	4.3%
CNR	2.0	3.5
Teflon HU Dev	56 HU	38 HU
Polystyrene HU Dev	11 HU	4 HU

Image Gentle mode (80kV, 100mAs)	FDK	iCBCT
Uniformity	92.0%	95.1%
Contrast	2.9%	2.9%
CNR	0.7	1.0
Teflon HU Dev	232 HU	226 HU
Polystyrene HU Dev	20 HU	0 HU

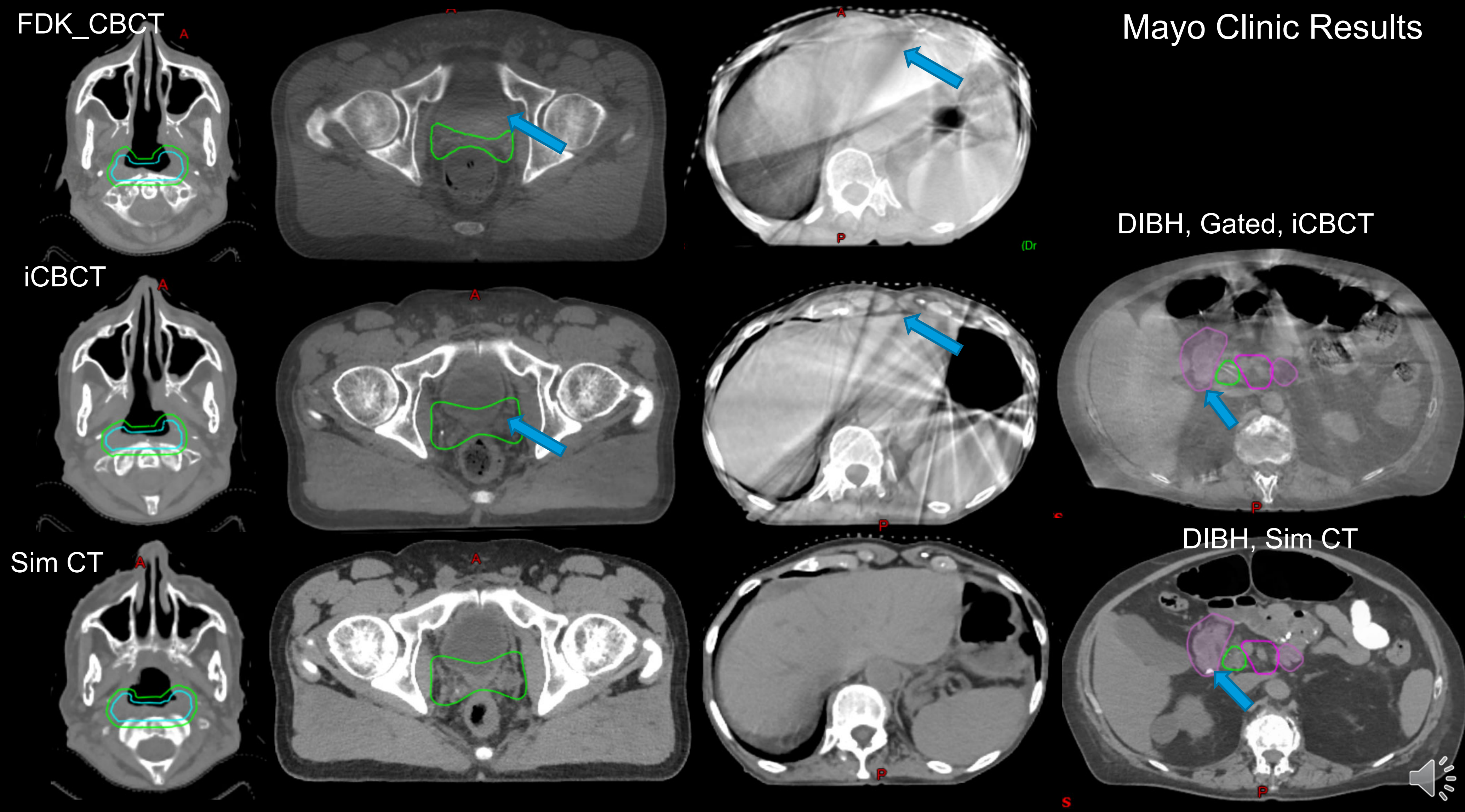
Pelvis (125kV, 270 mAs)

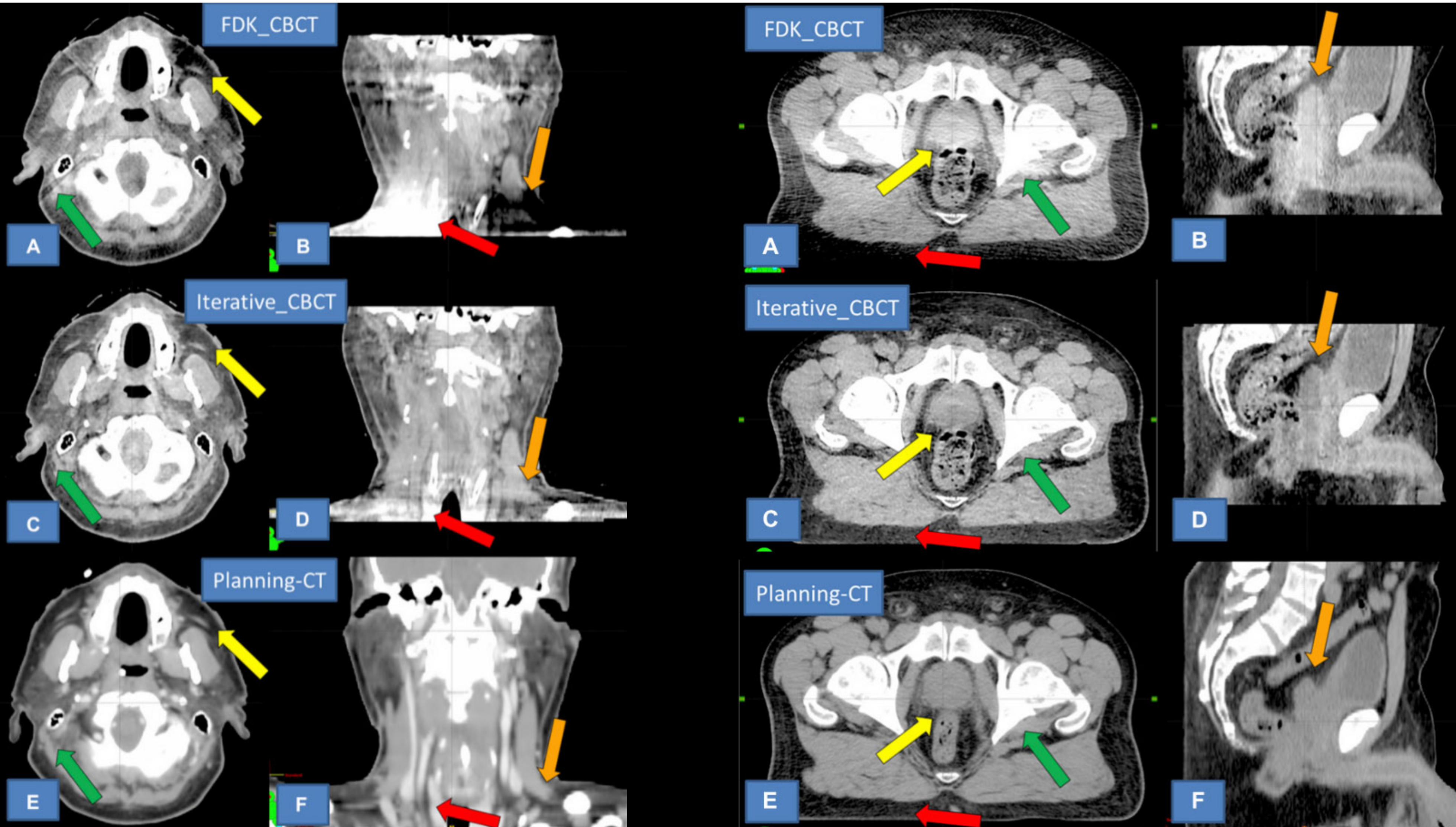


- ✓ Reduced noise
- ✓ Reduced streaky artifacts
- ✓ Increased uniformity with preserving edges

Pelvis (125kV, 1080 mAs)

Mayo Clinic Results





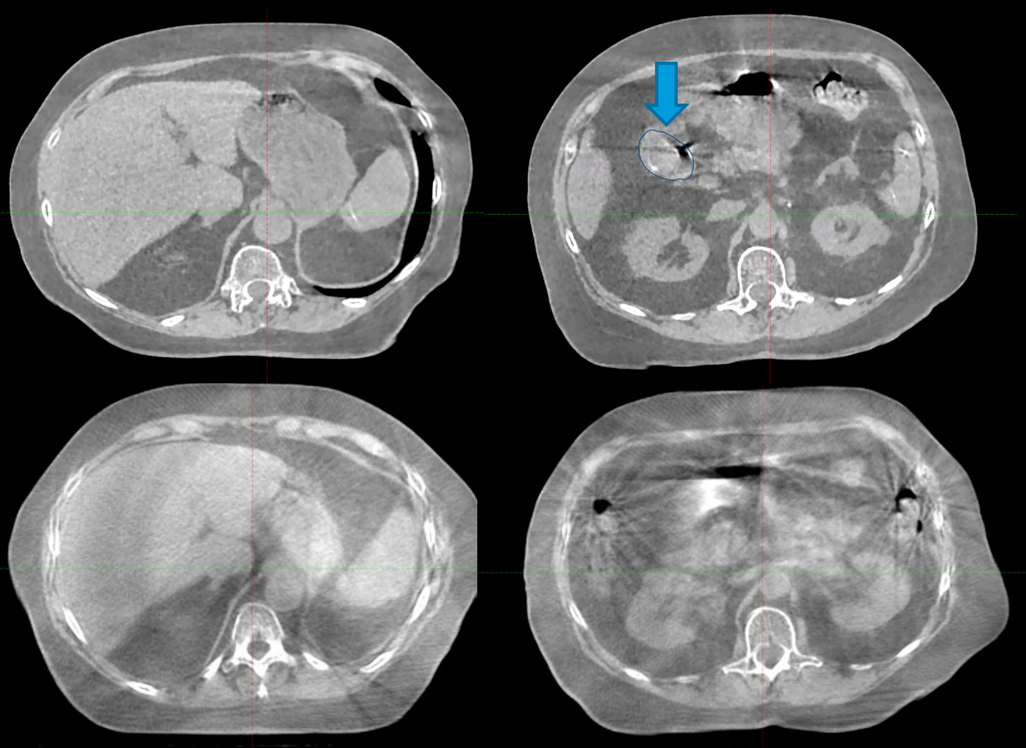
Gardner, Advances in Radiation Oncology, Volume 4, Issue 2, 2019, (Henry Ford)

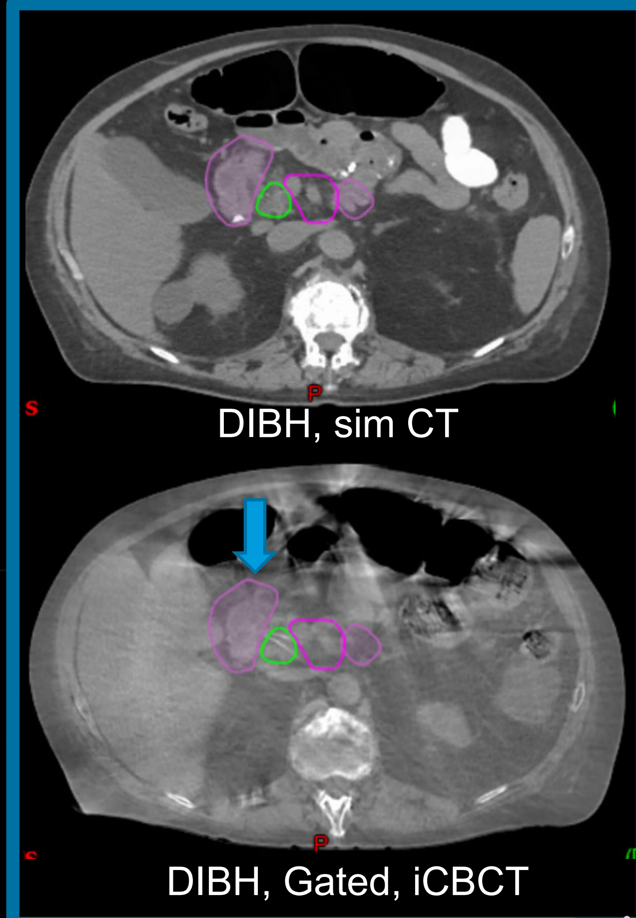
Cai, et al. Med. Phys. 46 (3), 2019.

Abdomen – Halcyon/Ethos vs TrueBeam

Halcyon CBCT exhale phase, single-breath hold

Truebeam CBCT Free-breathing

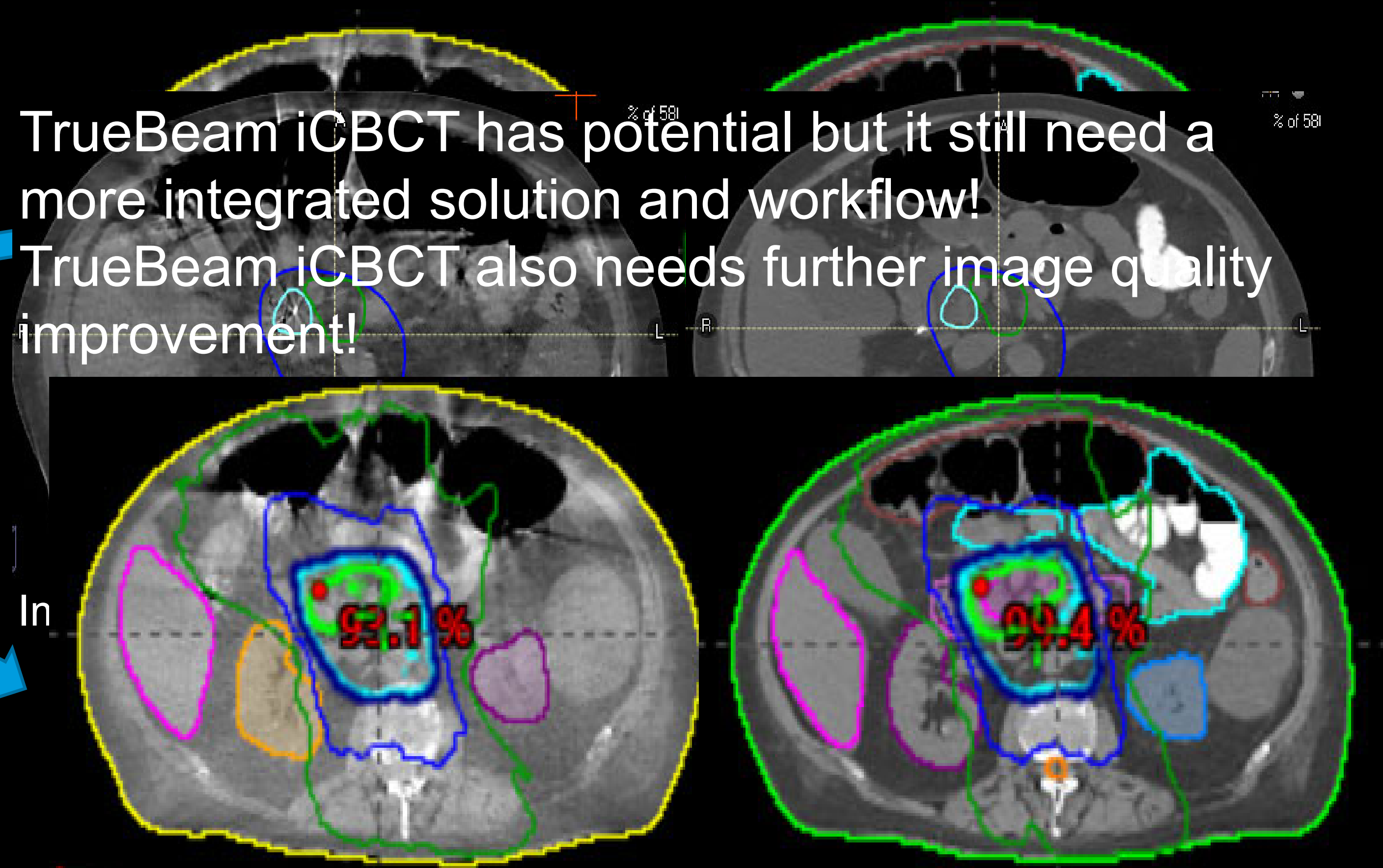




- ❑ Abdominal CBCT from TrueBeam with free breathing and Halcyon with breath-hold on expiration (25s scan time).
- ❑ TrueBeam gated iCBCT, improved image contrast, but still suffers from motion due to slow gantry rotation

Can we perform CTgART on TrueBeam?

- CT-resim
- Organ Auto-Segmentation
- Target Deformation
- Dose Verification
- Adaptive Treatment Planning
- Adaptive Treatment



TrueBeam iCBCT has potential but it still need a more integrated solution and workflow!
TrueBeam iCBCT also needs further image quality improvement!

Improved HU accuracy for dose verification

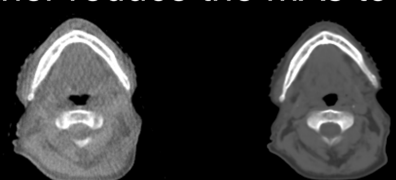
Deep-learning for improving CBCT image

- What areas need further improvement?
  - Motion artifacts: Pancreas tumor

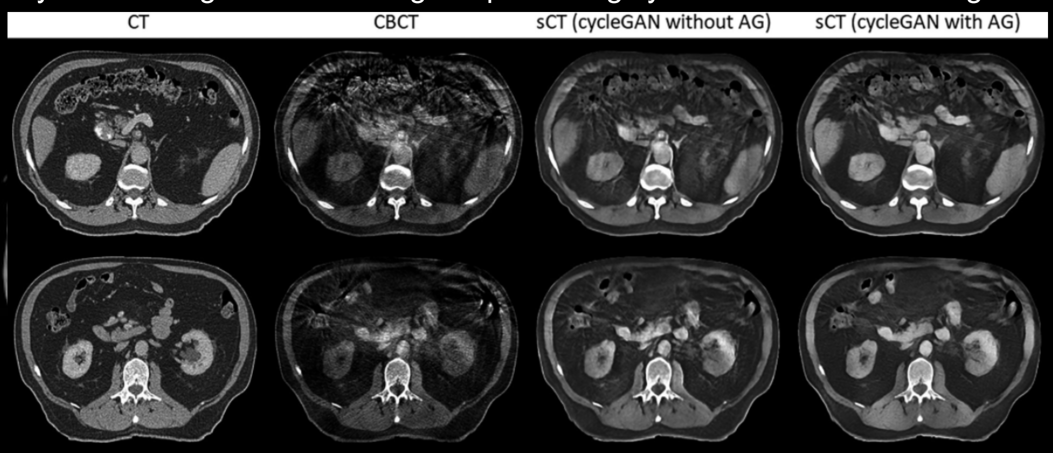
  Liu et al. Medical Physics, 47(6) 2020
  - Metal artifacts: Hip implants

  Ghani et. al., IEEE TCI, 6(181), 2020

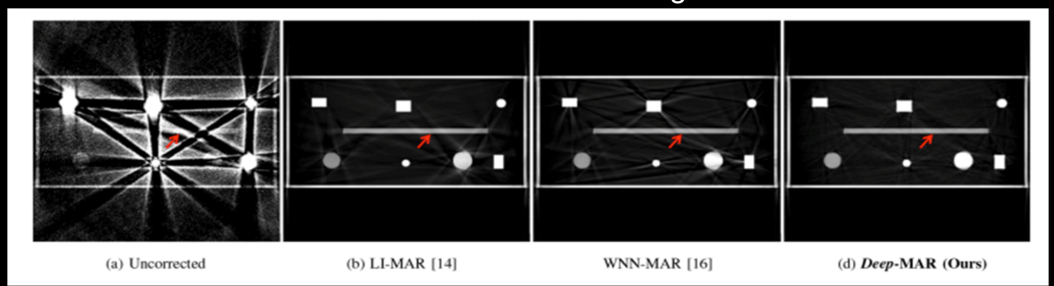
- What about low dose CBCT?
  - Image Gently calls for low-imaging dose for pediatric patients
  - Current Varian Image Gently protocol: 80 or 100kV, 93-100mAs, 460-490 projections
  - Could we further reduce the mAs to kV level?



Synthetic CT generation using deep-learning cycleGAN with attention gate



Fast Enhanced CT Metal Artifact Reduction Using Data Domain DL



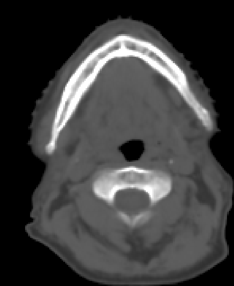
Deep-learning for Improving low dose CBCT

- Low dose fast scan CBCT: 10mA * 10ms per projection, 182 projections
- To train a deep convolutional neural network mapping original CBCT I_{oCBCT} to the co-registered high-quality CT images I_{CT}: $I_{CT} = f(I_{oCBCT})$
- The function f can be found by training a network via: $\min_{f} \| f(I_{oCBCT}) - I_{CT} \|$, with a global MAE loss function

$$Loss_{MAE} = \frac{1}{m \times n} \sum \sum \| I_{eCBCT} - I_{CT} \|_1 .$$

Dataset	Patient #
Patients with same-day CT and low dose CBCT (18mAs)	15 (5 for validation and 10 for testing)
Postoperative Patients, CT and first fx CBCT (18mAs)	40 (for training)
2D slice used for each patient	52
Total Training 2D Dataset	2080
Total Validation 2D Dataset	260

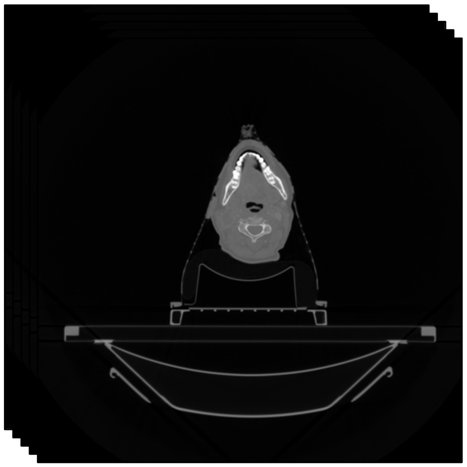
CBCT



CT

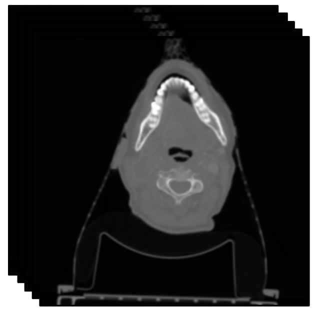
Yuan .....Rong. Phys Med Biol. 2020 Jan 27;65(3)

Pre-processing – Training Data & Labels



Original CT
512 x 512 x **126**

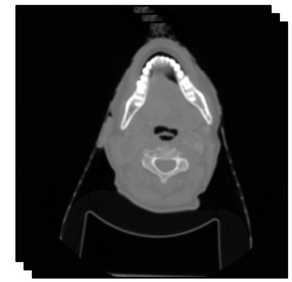
Registration



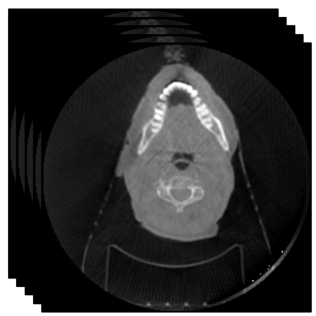
Aligned CT
270 x 270 x **88**

Clean outside of FOV

Crop the images

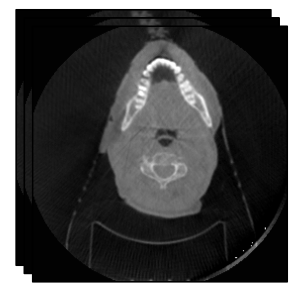


Resampled CT
256 x 256 x **52**



Original CBCT
270 x 270 x **88**

Crop the images

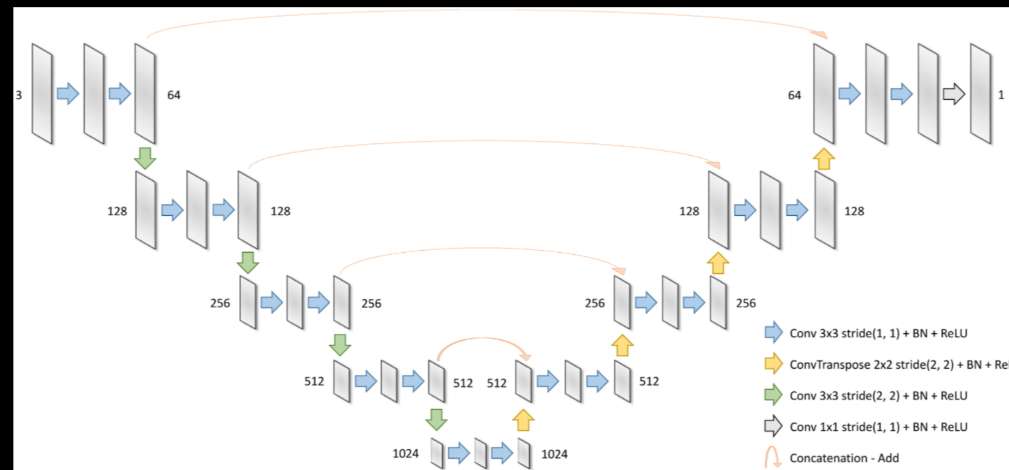


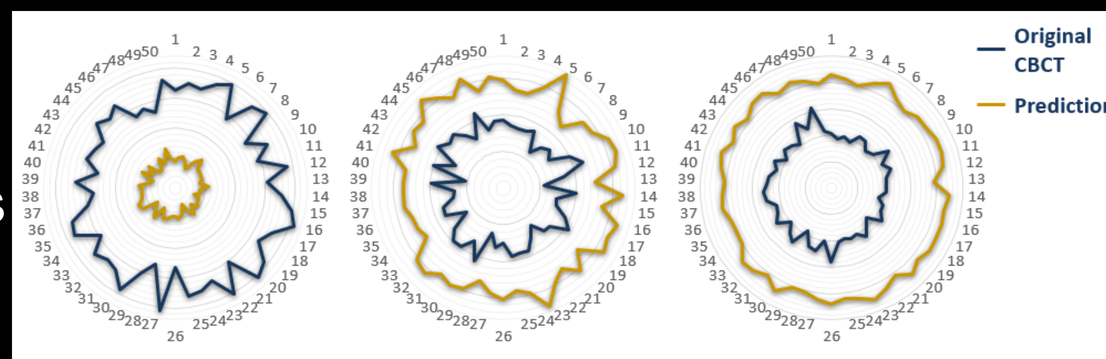
Resampled CBCT
256 x 256 x **52**

Helical CT: 120kVp tube voltage and around 400-500 mAs
CBCT: 100kVp voltage and only 18mAs exposure.

Quantitative Measures of Image Quality

- 2D U-Net architecture with 27-layers in 5 depths
- Comparing the enhanced CBCT (prediction) with the original CBCT, Improvement in average MAE from 172.73 to 49.28 HU, SNR from 8.27 to 14.25 dB, and SSIM from 0.42 to 0.85.
- The image processing time is 2 s per patient





(a) Mean Absolute Error (MAE)
167.46 HU to 49.24 HU

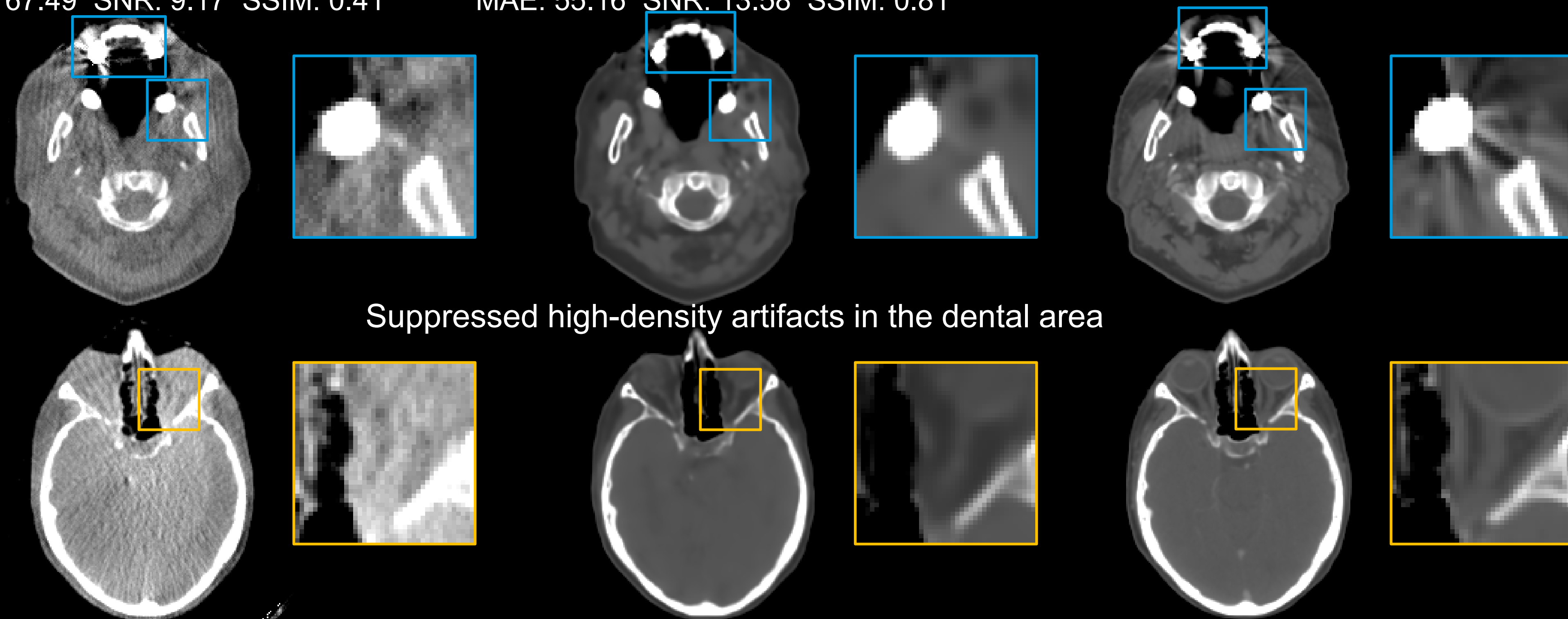
(b) Signal-to-Noise Ratio (SNR)
8.50 dB to 14.54 dB

(C) Structural Similarity (SSIM)
0.44 to 0.84

Soft Tissue Contrast Improvement

Original low-dose CBCT | Network Prediction | CT Reference

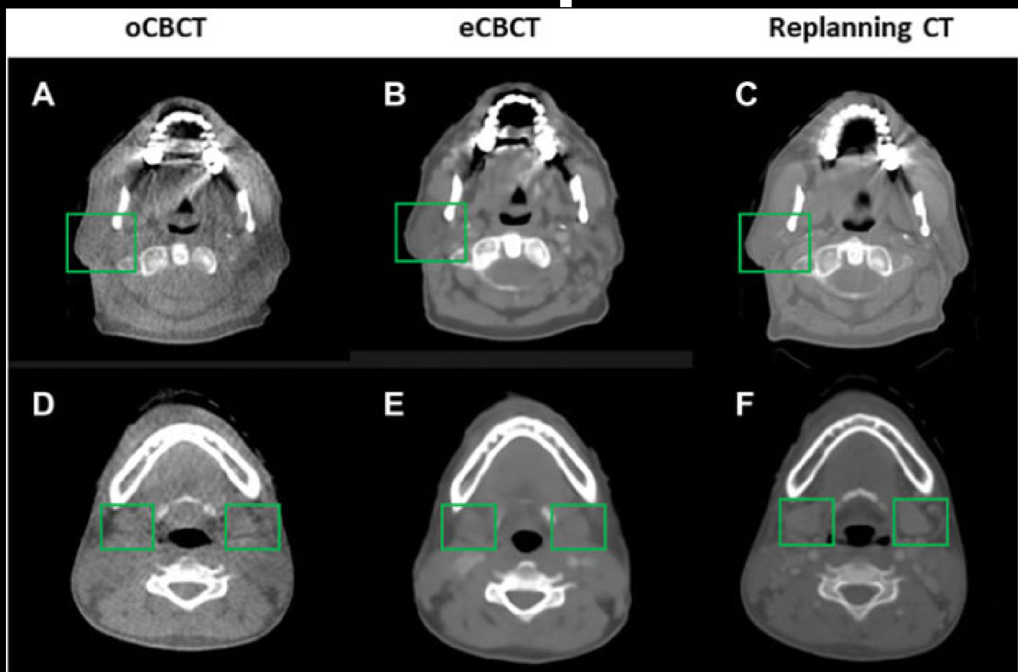
MAE: 167.49 SNR: 9.17 SSIM: 0.41 | MAE: 55.16 SNR: 13.58 SSIM: 0.81

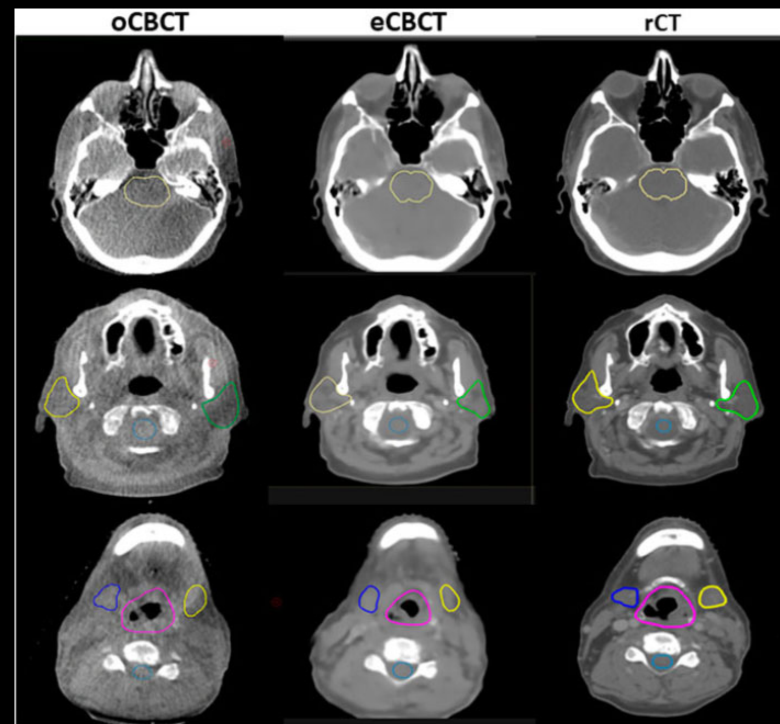


MAE: 181.00 SNR: 9.31 SSIM: 0.47 | **MAE: 42.88 SNR: 16.46 SSIM: 0.87** | Display window/level: 181/950

Lower image noise and less streak artifacts

Qualitative Improvement





- Lower image noise and less streak artifacts in the soft tissue region; suppressed high-density artifacts in the dental area; higher image contrast for parotid and submandibular gland areas
- Qualitative improvement for organ edge enhancement, facilitate contouring on eCBCT (brainstem, parotids, spinal cord, submandibular glands, and larynx)

Chen, … Rong. Frontiers in Artificial Intelligence. 2021 Feb*

Summary

- Three main factors are driving a paradigm shift in the field of radiation oncology
- More hypo-fractionation/SBRT treatments demand online-ART.
- Online-ART requires superior image quality, i.e. planning CT or MRI
- CBCT generated from a ring gantry and Acuros CTS-based iCBCT is being used for online-ART
- CBCT generated on a L-shape gantry (Truebeam) and Acuros CTS-based iCBCT has potential, but demands more practical solutions for an integrated workflow
- Deep-learning neural network has potential to further improve CBCT image quality, for challenging scenarios, i.e. low mAs images

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Thank You!