New Drugs &Technologies

5-Year Scan

Kiran Yemul, MHS
Oncology, Sg2

January 24, 2020
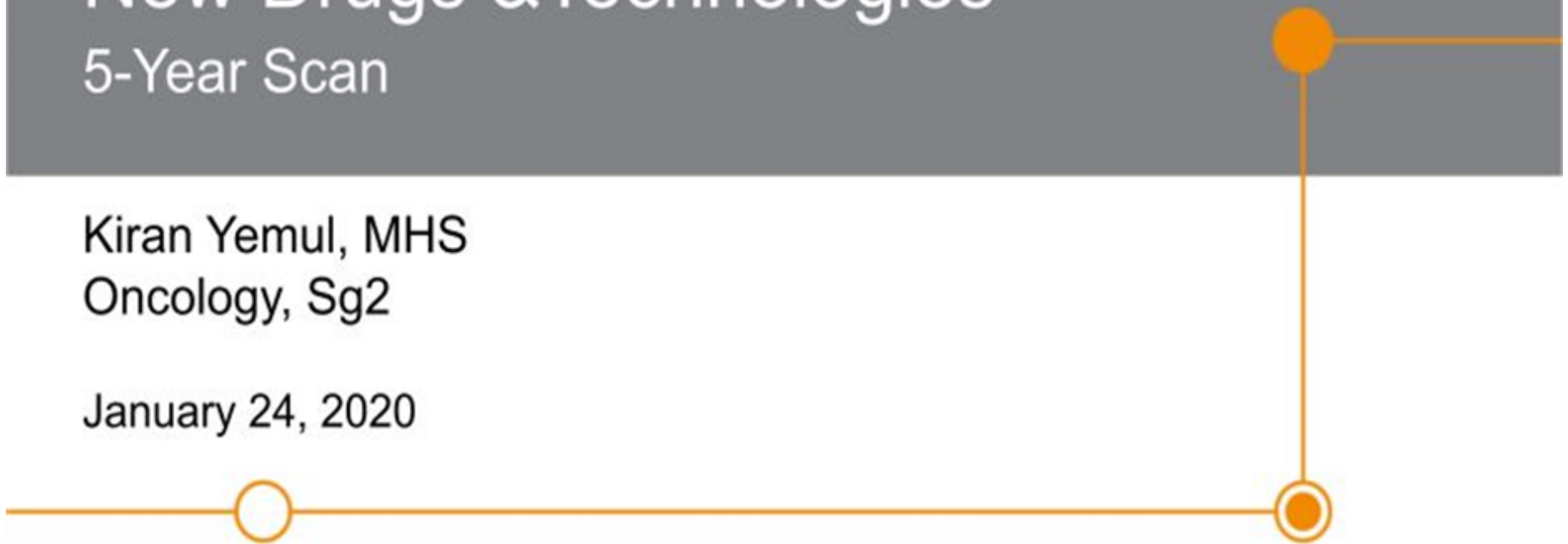
Agenda

CAR T-Cell Therapy

Artificial Intelligence

Adaptive Radiation Therapy

What's Next?

Successful Innovation Is…

Structured to match your organizational **culture**

Fully integrated into your organizational **strategy**

Answers the **critical questions**

Measure Return on New Technologies Across Four Strategic Levers

Bring **Care Model Innovations** to Market

Transform Cost Centers Into **Profit Centers**

Address **Key Questions**

Create **New Business Opportunities** Outside of the Core

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What's Next?

FDA Approved CAR T-cell Therapies Are Here, Additional Indications to Come

LEUKAPHERESIS

Collect patient's white blood cells

MANUFACTURING PROCESS

Isolate and activate T cells

Engineer T cells with CAR gene

Grow and expand number of T cells

INFUSION

Infuse same patient with engineered T cells

5-Year Impact

- Expanded availability, patient volumes
- Replace some BMT volume

ALL = acute lymphoblastic leukemia; NHL = non-Hodgkin lymphomas; MM = multiple myeloma; BMT = bone marrow transplant.
Source: Sg2 Impact of Change Forecast, 2019; figure: Dana Farber Cancer Institute.

Reimbursement for CAR T Is an Area of Ongoing Development…and Concern

August 2019, CMS final reimbursement and coverage determination released

Inpatient:

- NTAP increased from 50% to 65%
- Institutions still on the hook for at least $130,550 per case!
- No new MS-DRG for CAR T

Outpatient:

- ASP +6% = $395K for Yescarta and $503K for Kymriah

Commercial coverage usually via SCAs (with varying efficiency)

- Novartis: Money-back guarantee
- Spark Therapeutics: Rebates, bill payer directly, installment payments

Integrated

Memorial Sloan Kettering Cancer Center

- Consult service
- Leverage existing infrastructure for regulatory, cellular processing, clinical care delivery
- Benefits from optimized workflows e.g. data and quality management
- Centralized intake for BMT and commercial and investigational CAR T
- Avoid program redundancies
- Challenge: post-infusion management

Standalone

Seattle Cancer Care Alliance

- Cellular Immunotherapy Service
- Outpatient-based clinical care
- Dedicated clinical care team with enhanced expertise in the unique CAR T-cell toxicities
- Offer expanded outpatient hours
- IP care coordinated with BMT service
- Accommodates increasing patient volumes and eases the administrative burden on individual disease teams
- Challenges: cost, referral management

CAR T is Blazing the Trail for Other Innovative Immunotherapies

Bi-specific T-cell Engagers (BiTEs)

- Antibodies that bind T-cells to tumor cells
- Off-the-shelf treatment
- 2014: FDA approval for blinatumomab (Blincyto, Amgen) for ALL
- Clinical trials ongoing for expanded indications, solid tumor applications (prostate, CRC, melanoma)
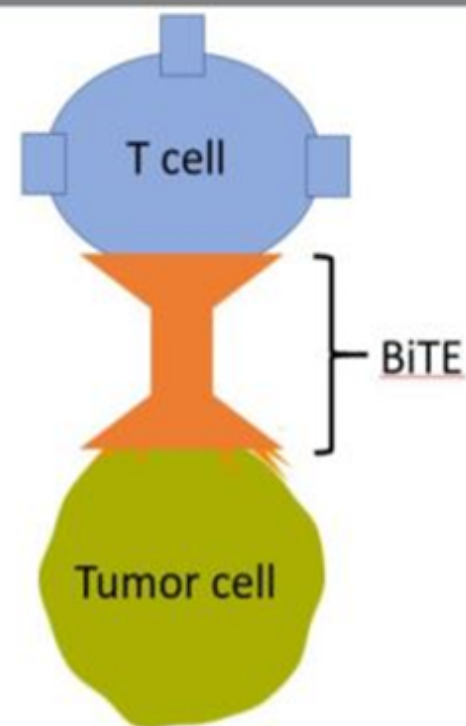
Key Takeaways

- Roadblocks to solid tumor CAR T are non-trivial
- Notable advantages of immunotherapies over traditional chemo and radiation
- Implementation challenges grease the wheels for other immunotherapies

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FDA APPROVALS FOR ARTIFICIAL INTELLIGENCE-BASED ALGORITHMS IN MEDICINE

Categories (right): CARDIOLOGY · PSYCHIATRY · ENDOCRINOLOGY · RADIOLOGY · GERIATRICS · NEUROLOGY · ORTHOPEDICS · EMERGENCY MEDICINE · OPHTHALMOLOGY · PATHOLOGY · ONCOLOGY

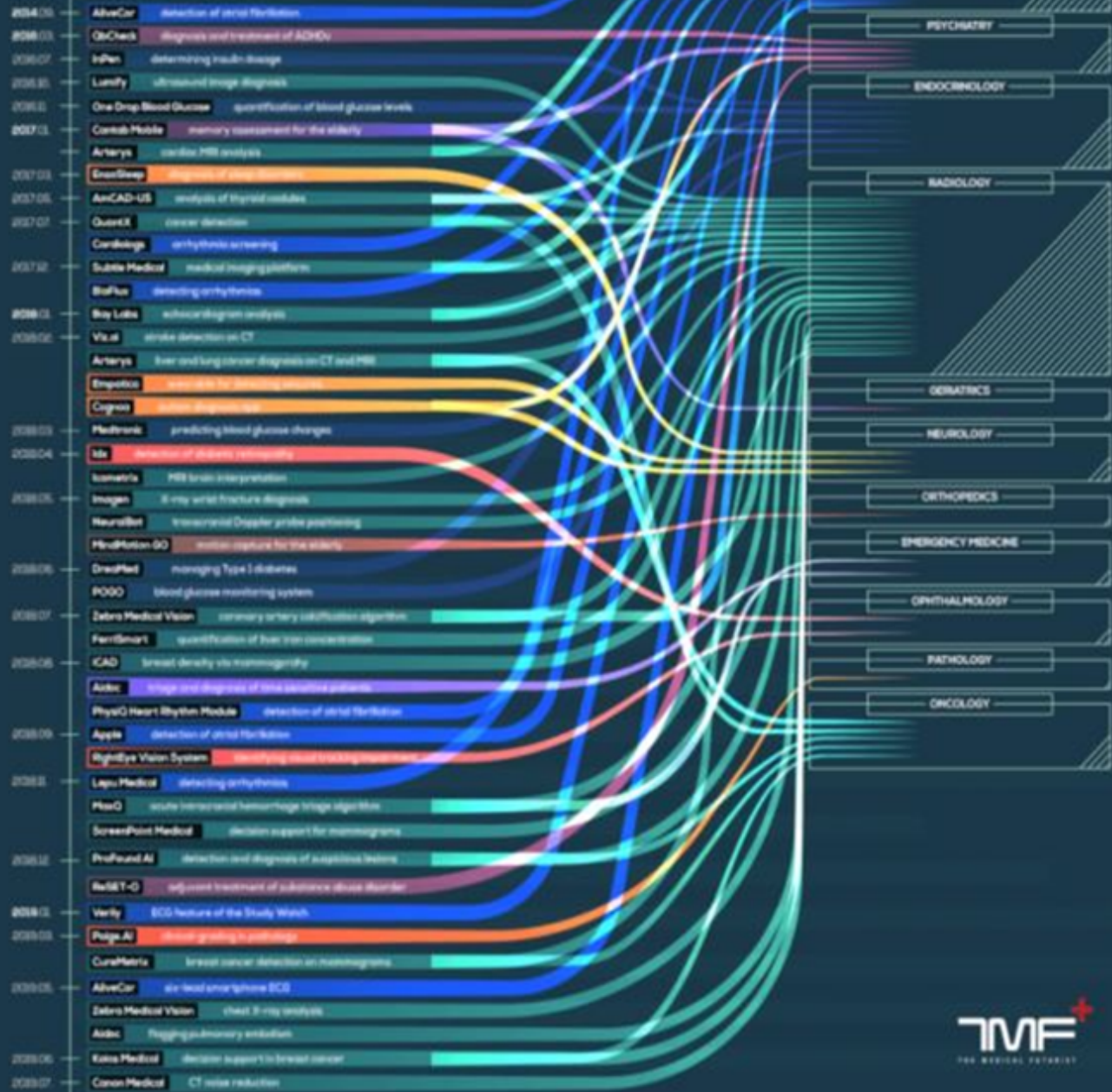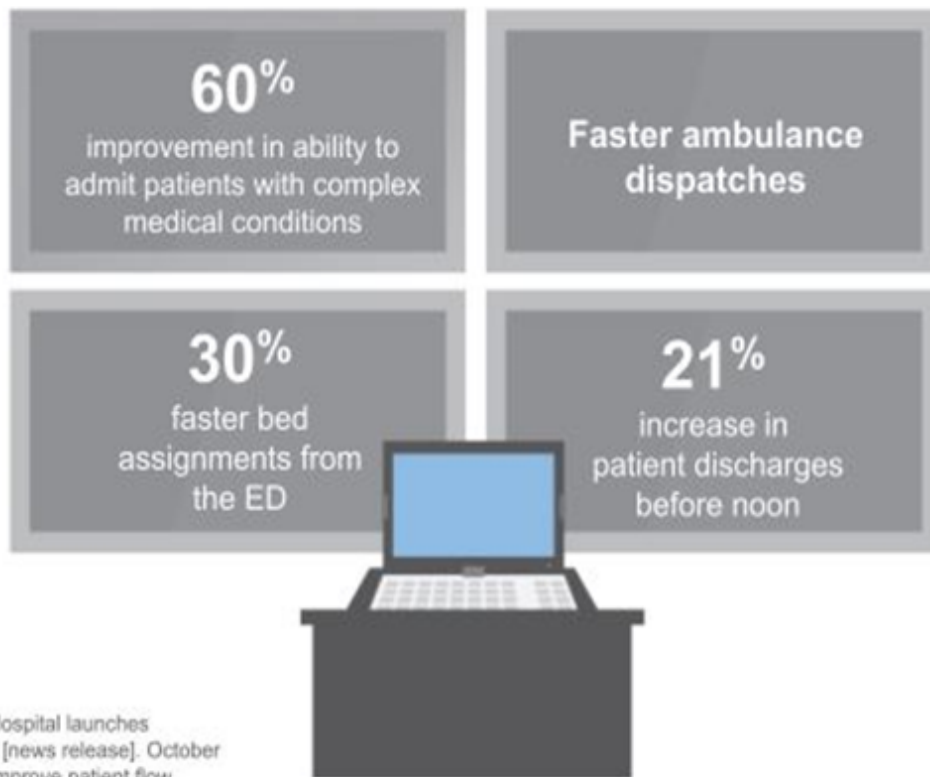| Date	Algorithm	Description
2014.03	AliveCor	detection of atrial fibrillation
2016.03	QbCheck	diagnosis and treatment of ADHD
2016.07	InPen	determining insulin dosage
2016.10	Lumify	ultrasound image diagnosis
2016.11	One Drop Blood Glucose	quantification of blood glucose levels
2017.01	Cerebb Mobile	memory assessment for the elderly
	Arterys	cardiac MRI analysis
2017.03	EnsoSleep	diagnosis of sleep disorders
2017.05	AmCAD-US	analysis of thyroid nodules
2017.07	QuantX	cancer detection
	Cardiologs	arrhythmia screening
2017.12	Subtle Medical	medical imaging platform
	BioFlux	detecting arrhythmias
2018.01	Bay Labs	echocardiogram analysis
2018.02	Viz.ai	stroke detection on CT
	Arterys	liver and lung cancer diagnosis on CT and MRI
	Empatica	wearable for detecting seizures
	Cognoa	autism diagnosis aid
2018.03	Medtronic	predicting blood glucose changes
2018.04	Idx	detection of diabetic retinopathy
	Icometrix	MRI brain interpretation
2018.05	Imagen	X-ray wrist fracture diagnosis
	NeuralBot	intracranial Doppler probe positioning
	MindMotion GO	motion capture for the elderly
2018.06	DreaMed	managing Type 1 diabetes
	POGO	blood glucose monitoring system
2018.07	Zebra Medical Vision	coronary artery calcification algorithm
	FerriSmart	quantification of liver iron concentration
2018.08	iCAD	breast density via mammography
	Aidoc	triage and diagnosis of time-sensitive patients
	PhysIQ Heart Rhythm Module	detection of atrial fibrillation
2018.09	Apple	detection of atrial fibrillation
	RightEye Vision System	identifying visual tracking impairment
2018.11	Lepu Medical	detecting arrhythmias
	MaxQ	acute intracranial hemorrhage triage algorithm
	ScreenPoint Medical	decision support for mammograms
2018.12	ProFound AI	detection and diagnosis of suspicious lesions
	reSET-O	adjunct treatment of substance abuse disorder
2019.01	Verily	ECG feature of the Study Watch
2019.03	Paige.AI	clinical grading in pathology
	CureMetrix	breast cancer detection on mammograms
2020.03	AliveCor	six-lead smartphone ECG
	Zebra Medical Vision	chest X-ray analysis
	Aidoc	flagging pulmonary embolism
2020.05	Koios Medical	decision support in breast cancer
2020.07	Canon Medical	CT noise reduction

CASE STUDY | AI Is Leveraged Today to Improve Operations

JOHNS HOPKINS HOSPITAL, BALTIMORE, MD

Partnered with GE Healthcare to develop an AI-driven command center

60% improvement in ability to admit patients with complex medical conditions

Faster ambulance dispatches

30% faster bed assignments from the ED

21% increase in patient discharges before noon

Sources: Johns Hopkins Medicine. The Johns Hopkins Hospital launches capacity command center to enhance hospital operations [news release]. October 26, 2016; Johns Hopkins Medicine. Command center to improve patient flow. *Insight.* March 2016; Slabodkin G. Johns Hopkins Hospital command center is first of its kind. HealthData Management. January 24, 2017.

| AI for Risk Prediction and Care Planning

ABRAMSON CANCER CENTER, UNIVERSITY OF PENNSYLVANIA

Situation

- Providers challenged to initiate end of life care conversations

Solution

- Developed AI to predict the risk of -month mortality risk among cancer pa...

- Integrated EHR notifications encouraged physicians to initiate care planning conversations

IMPACT

- Palliative care consultation increased by **74 percent**

- Anticipated savings for health systems via reduced spending on noncurative chemotherapy and other maintenance therapies

Source: Parikh RB, et al. *JAMA Oncology*, 25 Oct 2019; Machine Learning Approaches to Predict 6-Month Mortality Among Patients With Cancer, 2(10):e1915997.

Artificial Intelligence Is Making A Move Into Radiation Therapy Treatment Planning

AI Works Alongside Doctors to Improve Radiation Treatment Planning Process

- Quickly differentiate tumor versus healthy tissue for every image
- Easily performs OAR analysis
- Rely on database of previous treatment plans
- Develop machine learning algorithms
- Workflow efficiency substantially improves

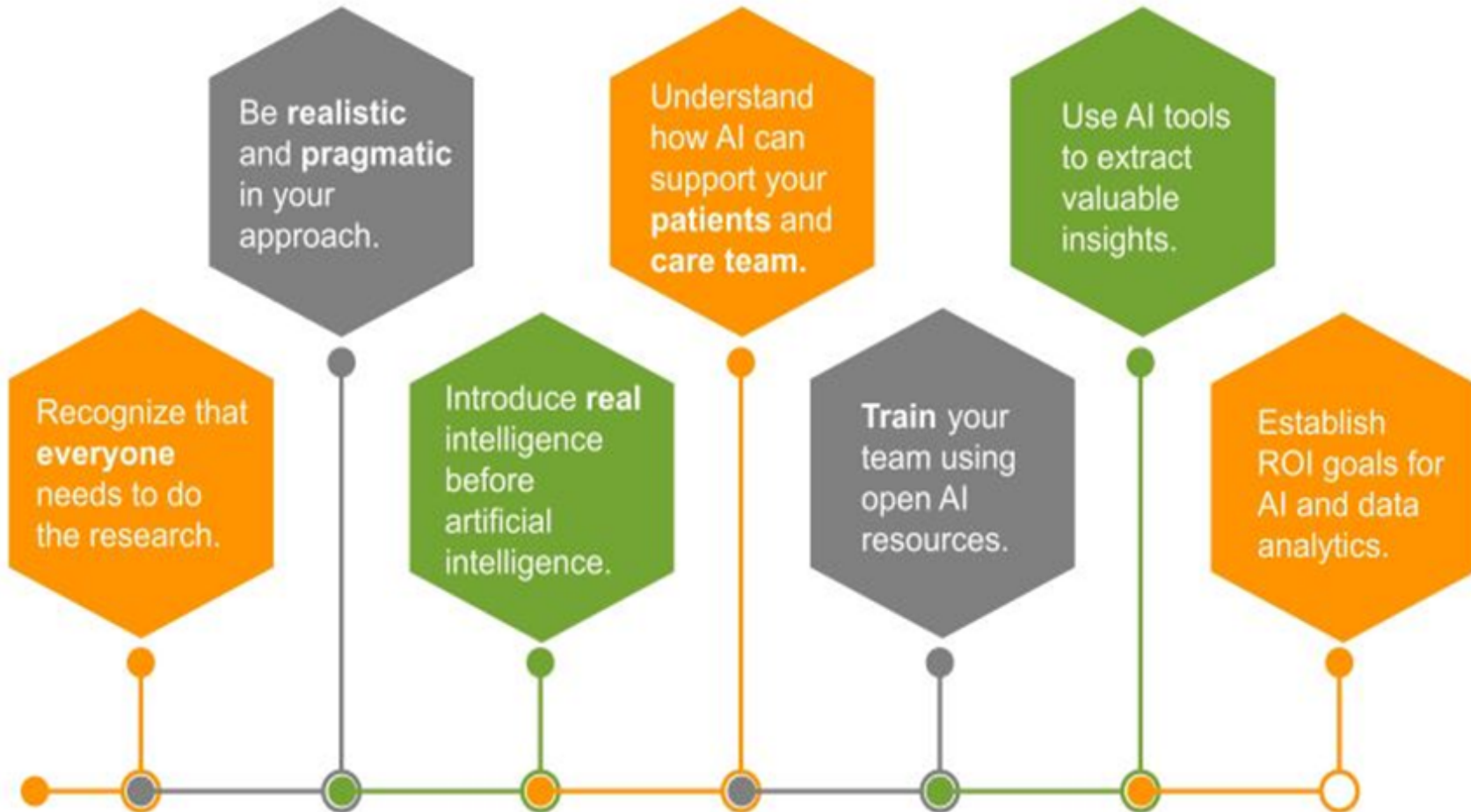| RaySearch	Microsoft	Google
RayStation/UHN	**InnerEye/Addenbrooke**	**DeepMind Health/UCLH**
▪ Uses machine learning and image processing from thousands of previous plans ▪ Integrated into existing RayStation platform	▪ Assistive AI to treat cancer and monitor progress ▪ Goal is to have AI do 95% of work and shorten time from hours to minutes	▪ Partnership to develop new treatment planning tool ▪ 700 former head/neck patients ▪ 75% reduction in treatment planning time to 1hr

OAR = organs at risk; **UCLH** = University College London Hospital; **UHN** = University Health Network
Sources: University College London Hospital; RaySearch Laboratories; Project InnerEye, Microsoft; Google DeepMind Health, LLC.

7 Steps to Prepare for Artificial Intelligence Today

Be **realistic** and **pragmatic** in your approach.

Understand how AI can support your **patients** and **care team.**

Use AI tools to extract valuable insights.

Recognize that **everyone** needs to do the research.

Introduce **real** intelligence before artificial intelligence.

Train your team using open AI resources.

Establish ROI goals for AI and data analytics.

Focus on the conversation and the technology disappears.

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What's Next?

Adaptive Radiation Therapy Allows for More Precise Treatment Delivery

Adapt treatment in response to changes in size, position, and shape of tumors and organs at risk

Adaptive Radiation Therapy (ART)

- Image guidance

- Treatment adaptation

  - Patient repositioning

  - Treatment re-planning/re-optimization

- Dose verification

- Useful in difficult to treat regions - head & neck, pancreas, prostate

5-Year Impact

- Expanded availability of IGRT and ART, new market entrants
- AI meets ART

Sources: Lamb J et al. Cureus. Online Adaptive Radiation Therapy: Implementation of a New Process of Care, 2017 Aug; 9(8): e1618; LI T, Towards the Clinical Implementation of Online Adaptive Radiation Therapy for Prostate Cancer, 2013; Zagoudis J, Imaging Technology News, 29 May 2019, Advances in Radiation Therapy Treatment Systems.; Sg2 Analysis, 2019.

MR-Guided Radiotherapy Has Become a Reality

- Concept announced in 2002; first system installed at UMC Utrecht in 2014
- Real-time, continuous MR imaging during treatment
- Adaptive, on-bed radiation therapy planning
- MR-guided radiotherapy is particularly beneficial for soft tissue tumors, tumors near critical structures, and accurate gating and tumor movement.
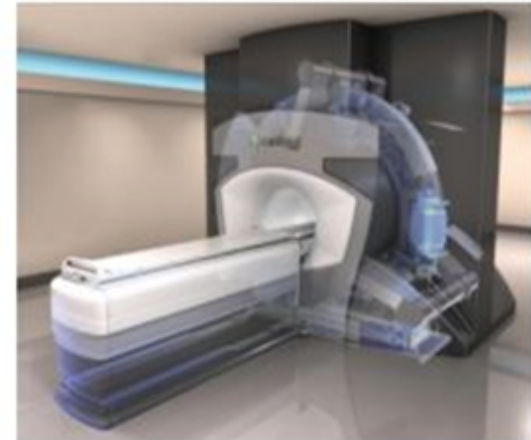

Image courtesy of ViewRay.

ViewRay—MRIdian(LINAC)

- 6 MV linear accelerator, 0.35T MR
- FDA cleared (2012, 2017)
- Installed at BJH, UCLA, UWisc
  - BJH: breast (18%), lung (14%), colorectal (13%), bladder (12%), prostate (5%)

Elekta/Philips—Unity

- 6 MV linear accelerator and 1.5T MR
- 7 member Atlantic Research Consortium includes 2 US facilities: MD Anderson, Froedtert/MCOW
- Early projections
  - 75 orders expected by EOY 2019; costs $8 - $10M

BJH = Barnes-Jewish Hospital; MCOW = Medical College of Wisconsin; MR = magnetic resonance; UCLA = University of California Los Angeles; UMC = University Medical Center; UW = University of Wisconsin

Turning Cancer Against Itself With Biology-guided Radiation Therapy

RefleXion Medical; Biology-guided Radiotherapy (BgRT)

- LINAC with PET emission detectors for IMRT and stereotactic radiation delivery
- Delivers beamlet of radiation in response to each tracer emission along the line of response (LOR)
- Dynamic real-time tracking; same session treatment for multiple mets
- Reduced treatment margins and lower radiation dose to healthy tissue

"Tumors continuously signal their location during treatment"

Linac = linear accelerator; mets = metastatic cancer.
Sources: ReleXion Medical website https://www.reflexion.com/; ASTRO 2018.

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What's Next?

Extras: What Else to Watch for in 2020 and Beyond

1. Expanding indications for liquid biopsy
2. New applications for cancer vaccines
3. Clinical trial data on proton therapy
4. Direct-to-consumer genetic risk assessment
5. Direct-to-consumer cancer screening
6. New PET radiotracers and better availability
7. *In silico* cancer drug trials
8. At-home lab marker measurement
9. New wearable therapeutics (e.g. brain cancer, pain management)

Wrap Up: What's Next?

- As CAR T-cell demand and indications will grow, look for future developments in reimbursement landscape

- Position your organization on the AI learning curve by understanding how AI can support your patients and care teams

- Empower providers with "precision" radiation oncology tools e.g. adaptive radiation therapy technologies

- Prepare for direct-to-consumer cancer offerings that will disrupt traditional service offerings

Questions?

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Our analytics and expertise help hospitals and health systems achieve sustainable growth and ensure ongoing market relevance through the development of an effective System of CARE.

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Your 100-Day Plan in 7 Steps

1. Rank in priority order your patient interactions by how critical they are to your current revenue and future growth.

2. Pick the top 3 to 5 interactions and work with your service line and product teams to streamline patient engagement with your most important services. This process will help identify areas where AI can improve future interactions.

3. Identify what information and insights you lack that would help you improve the patient experience. Design your AI tools to help access and use and to provide key insights to you and your patients.

4. Develop AI personas that fit your brand and communicate your brand voice.

5. Begin adding sophistication to your digital interactions. Consider piloting AI in roles like content curator (for personalization) or interaction advisor (for intelligent automation). These new roles should accompany the patient along their various journeys.

6. Identify communication channels and platforms for integrating conversational experiences with your brand. Consider internal as well as external interactions.

7. Gather and review existing key performance indicators (KPIs) for patient success. Ensure these KPIs account for the benefits of simplified interactions.