digital imaging
and anatomic pathology’s care delivery model

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1 disruptive innovation
what differentiates it from sustaining innovation?

2 digital pathology
just how disruptive is it? what trends will it trigger?

2 10 trends for 2020
how will the delivery model change? and why?
what is a **disruptive** innovation?
what is this?
a low-end car?
Building the world's cheapest car
The cheapest car in the world, set to sell for just $2,500, is being unveiled at the Delhi Auto Expo by the Indian car manufacturer, Tata Motors. The "one lakh"—slang for 100,000 rupees—people's car is aimed at the country's 60 million scooter riders currently unable to afford a car.

Rear-mounted engine:
Two-cylinder petrol, 660cc, 135hp, built by Bosch

Fuel efficiency: 60mpg
Top speed: 75mph
0-50mph: 21 secs

Front luggage compartment:
Holds battery, windshield washer bottle, room for single suitcase

Rear wheel drive:
Uses continuous variable transmission, lighter alternative to manual or automatic

Cost saving:
No radio, power steering, air conditioning, emissions control, antilock brakes, air bags, safety beams

Single windscreen wiper

Weight savings:
Extensive use of plastic

Wheel bearings:
Strong enough to drive car at 45mph, but will visibly wobble at higher speeds

a high-end motorcycle?
a low-end ultrasound?

a high-end stethoscope?
what is this?
Another disruptive innovation

These innovations were all disruptive for a single reason:

When they were introduced, their performance was initially much lower than that of the existing technologies...

But, they were able to bring the cost down so dramatically that their adoption became inevitable... sometimes in an alternative market segment (to start with)

Eventually, their performance caught on, and led to their mass dissemination.
now, another type of disruptive innovation
These innovations were also disruptive, but for a different reason:

They were able to “deconstruct” the existing value chain of a business…

They were able to “dis-intermediate” the value chain of a business…

They were able to “re-configure” the value chain with a different set of players.

Their adoption was set off by some “tipping point”

all great examples of disruptive innovation
but, in order to see why,

we had to look

unconventionally

In the conventional world of “looking”,

it is easy to see what is going on,
reality is recognizable,
even though sometimes fuzzy, the picture is understandable.
Then things start to look funny …

they become harder to recognize
... and disjointed,

... but you can still tell what is going on.
However, it gets harder…

... and harder
and finally it becomes impossible

to see what is going on...
… by looking at things the **conventional** way.
our onus is to figure out the pattern

that lies hidden underneath the apparent chaos on the surface

to see through Picasso’s outer shell and uncover...
our onus is to figure out the pattern
space :: pattern
time :: trend

trends
two trends triggered by disruptive innovation

2 things you simply could not do at all before

1 things you can do at a significantly lower cost
what did digital-ization transform in radiology?

31,567 asymptomatic persons at risk for lung cancer using low-dose CT identified 484 with stage I lung cancer

Surgery improved five-year survival

ca 1900
X- Ray

ca 2000
CT
15 years of digital radiology

- Productivity up by 20%
- Report turn-around time down from 3 days to 3 hours
- Radiology study availability up from 60% to nearly 100%
- "Handling errors" down – undocumented
- Clinician viewing up by a factor of 2
- Comparison with prior studies up by a factor of 5
- Screening (breast, lung, colon) up by a factor of 10

New:
- 3D Visualization
- Quantitative analysis (Cardiology, Oncology)
- Fusion – anatomy and physiology
- Contextual access to anatomy atlas at POC
- Contextual access to “similar cases” at POC
- Contextual access to expert opinion at POC

2 things you simply could not do at all before

1 things you can do at a significantly lower cost
2 redefine standard of care

1 automate standard of care

what did digital-ization transform in radiology?
what can digital-ization
transform in pathology?

Potential Clinical Use Cases... inventoried

- quantitative comparison
- improve report turnaround time
- case sharing and collaboration
- pathology 2.0
- education
- archiving and retrieval
- tumor boards
- remote case review
- reporting
- improve slide “availability”
- efficient primary diagnosis
- consultation and second opinions
- research and clinical trials
- reduce handling errors
- data mining for decision support
- quantification
- CME and proficiency testing
- remote frozen sections
- QA
- companion algorithms
- image analysis
- improve slide “availability”
- personalized medicine
Potential Clinical Use Cases... organized

Quantitative comparison
Case sharing and collaboration
Image analysis
Remote frozen sections
Data mining for decision support
Personalized Medicine

Improve report turn-around time
Archiving and retrieval
Tumor boards
Remote case review
Efficient primary diagnosis
Reduce handling errors
Improve slide availability
Quantification

1
2

Quantitative comparison
Case sharing and collaboration
Image analysis
Remote frozen sections
Data mining for decision support
Personalized Medicine
1. **things**
   - you can do at a significantly lower cost

2. **things**
   - you simply could not do at all before

1. **automate**
   - standard of care

2. **redefine**
   - standard of care
how do we implement digital pathology?
companion algorithms™

software applications

scanners
companion algorithms™

software applications

scanners
Digital Pathology?

- scanners
- software applications
- companion algorithms™
companion algorithms ™
ER/PR IHC: Nuclear Algorithm

<table>
<thead>
<tr>
<th>Results</th>
<th>Nuclear</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Stained Cell Count</td>
<td>96</td>
</tr>
<tr>
<td>Stained Cell Count</td>
<td>314</td>
</tr>
<tr>
<td>Percent Positivity</td>
<td>77</td>
</tr>
</tbody>
</table>

Cytoplasmic Algorithm
Digital Scoring of Her2-neu FISH

- Dark red: large cluster (+)
- Light red: small cluster (+)
- Blue: polysomy (-)
- Green: Nucleus diploid (-)

Final: 154 nuclei—51 single, 21 polysomy, 41 small+, 41 large+

Digital Scoring of Her2-neu CISH

- Dark red: large cluster (+)
- Light red: small cluster (+)
- Blue: polysomy (-)
- Green: Nucleus diploid (-)

Final: 154 nuclei—51 single, 21 polysomy, 41 small+, 41 large+
Prostate Panel: IHC triple stain algorithm

P504s (red, cytoplasmic stain)
K903 (brown, cytoplasmic stain)
p63 (brown, nuclear stain)

Red glands (Red only): Adenocarcinoma
Green glands (Brown only): Benign
Yellow glands (Red + Brown): HGPIN
Ki67 Scoring in CNS Glial Tumors

Companion Algorithms: Breast Cancer

Her2-neu IHC, FISH, and CISH: selection of patients for Herceptin®

ER/PR scoring selection of patients for anti-estrogen therapy
Companion Algorithms: Colon and Lung

Colon Cancer
- EGFR testing (IHC/FISH) for selection of patients for Erbitux®
- Thymidylate synthase testing for selection of patients for anti-folate based chemotherapy
- MLH/MSH testing for identification of patients with hereditary nonpolyposis colorectal cancer (HNPCC)

Lung cancer
- EGFR testing (IHC/FISH) for selection of patients for Tarceva® and Iressa®
- ERCC1 and RRM1 testing (IHC) for selection of patients suitable for chemotherapy drugs - prediction of response to cisplatin and gemcitabine

Companion Algorithms: Other Cancers

Prostate Cancer
- Therapy selection - AR IHC for selection of patients for anti-androgen therapy
- Prognostic FISH markers - 21q22 Rearrangements (TMPRSS2)

Gastrointestinal Stromal Tumors
- CD117 testing for diagnosis and selection of patients for Gleevec® therapy

Oligodendrogliomas
- FISH testing for deletions at chromosomes 1p and/or 19q for predicting response to chemotherapy

Lymphomas/leukemias – variety of tests (including IHC and FISH) crucial for diagnosis, prognosis, and treatment decisions
companion algorithms™ enable companion diagnostics

companion algorithms™ enable personalized medicine
Personalized Medicine: What?

Enable Personalized Medicine
“What diagnosis/care would be optimal for this patient”

Key Enabler
“Emergent”
Knowledge

Support evidence-based medicine
“How should patient be treated per guidelines”

Personalized Medicine: How?

1. **Collection** of large databases of patient data and external medical knowledge

2. **Creation** of personalized knowledge models

3. **Application** of personalized knowledge models in clinical workflow
Personalized Medicine: How specifically?

Probabilistic Inference Over Time

Clinical Decision Support Application

Combine Conflicting Local Evidence

Probabilistic Inference Over Time

Extraction

Extraction

Extraction

Pathology Images

Genomics

Proteomics

Lab Pharmacy Text Notes

Radiology Images

Personalized Knowledge Models

Pathology... … is a key “missing piece”

digital pathology...
Identification of biomarkers whose expression correlates with:

1. Behavior of disease (for prognosis)
2. Response of disease to specific therapeutic agents

... the role of quantification will increase
companion algorithms™
will redefine standards of care

how do we accelerate
adoption?
Case of the Week
Tumor in the right colon

Join the community!
We are currently accepting new members. Sign up for FREE to see what the buzz is all about!

Browse interesting cases from around the world
Create your own online case gallery
Share your cases and slides with colleagues
Search over expanding global knowledge base
Learn about the latest advances
Ask for advice for your opinion on your case

Browse case gallery
Browse cases in a category

Browse a case
Browse digital slides

Browse similar cases
Create a case

Scan slides and upload
Create your own case gallery

Search for cases, users...
250 days... since launch
4000 pathologists... online
8000 cases... uploaded
120 countries

what is our compass?
Our compass for the industry:

1. … from acquisition thru image analysis, to decision support to report
2. … from “off-time” to real-time, from single-modality to multi-modality
3. … from morphology to molecules (…morphology AND molecules)
4. … from “information” to “diagnostic confidence”
5. … to personalized medicine, enabled with companion algorithms™

What does that mean?

“from pathologist to diagnostician”

… an INTEGRATOR!

what trends will this trigger...
... for the delivery model

1 integration across the value chain
2 disintermediation of the value chain

3 personalization of therapeutic decisions
4 super-specialty
based delivery model

5 integration
of morphology and molecules
6 integration
radiology and pathology

7 integration
across the medical record
efficiency will remain a key driver

informatics will emerge as a “practice”
education will change dramatically

Digital Pathology will....

1 automate standards of care

2 redefine standards of care
And we are at....

the end of the beginning

real thing

beginning
innovation

trend

digital pathology
an enabler for a disruptive change
digital pathology
the beginning of a trend