IRE
ISTITUTO NAZIONALE TUMORI
REGINA ELENA
ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO

Adding "precision" to surgical treatments

(15 minutes)

Gian Luca Grazi

Hepato-Biliary-Pancreatic Surgery

National Cancer Institute *Regina Elena*

Rome

Modern concept of surgical oncology

- ✓ As surgeons acquired a better understanding of surgical anatomy and physiology, perioperative management improved, surgery expanded and training programs developed.
- ✓ Modern surgery demonstrates potentially curative treatment options when facing a patient with tumors including ablative techniques, open or minimal access surgery, and organ transplantation.
- ✓ Preoperative selection of the therapeutic approach should consider the staging of primary cancer, concomitant diseases, and the patient's performance status.
- ✓ A twenty-one-century surgeon must be equipped with excellent theoretical and clinical skills to perform a precise operation.
- ✓ Modern surgeons need to acquire high-level knowledge about the various surgical procedures and techniques available to perform a oncological correct procedure.

Modern concept of surgical oncology

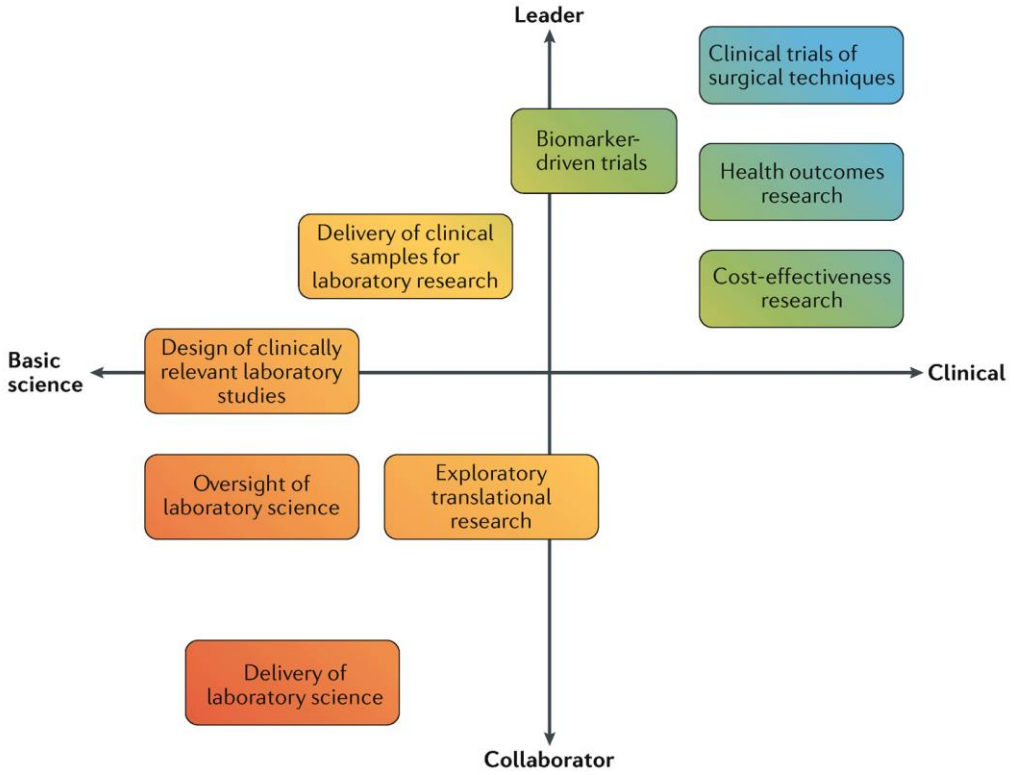
PERSPECTIVES

OPINION

Reshaping the critical role of surgeons in oncology research

Robert. P. Jones, Chandrakanth Are, Thomas J. Hugh, Dirk J. Grünhagen, Jianmin Xu, Charles M. Balch and Graeme J. Poston

Abstract | Surgery remains a mainstay in the treatment of most solid cancers. Surgeons have always engaged in various forms of high-quality cancer research to optimize outcomes for their patients, for example, contributing to clinical research and outcomes research as well as health education and public health policy. Over the past decade, however, concerns have been raised about a global decline in the number of surgeons performing basic science research alongside clinical activity — so-called surgeon scientists. Herein, we describe some of the unique obstacles faced by contemporary trainee and practising surgeons engaged in research, as well as providing a perspective on the implications of the diminishing prominence of the surgeon scientist. Finally, we offer some thoughts on potential strategies and future directions for surgical engagement in oncology research to increase the number of research-active surgeons.



Potential roles of surgeons in oncology research. Surgical engagement in cancer research can take many forms. Research can vary from basic laboratory science through to purely clinical studies and, depending on the type of research involved, can require surgeons to adopt a leadership or more collaborative role. The precise definition of these roles will vary depending on each unique team and research scenario, although a selection of possible surgical oncology research engagements are illustrated in the figure.

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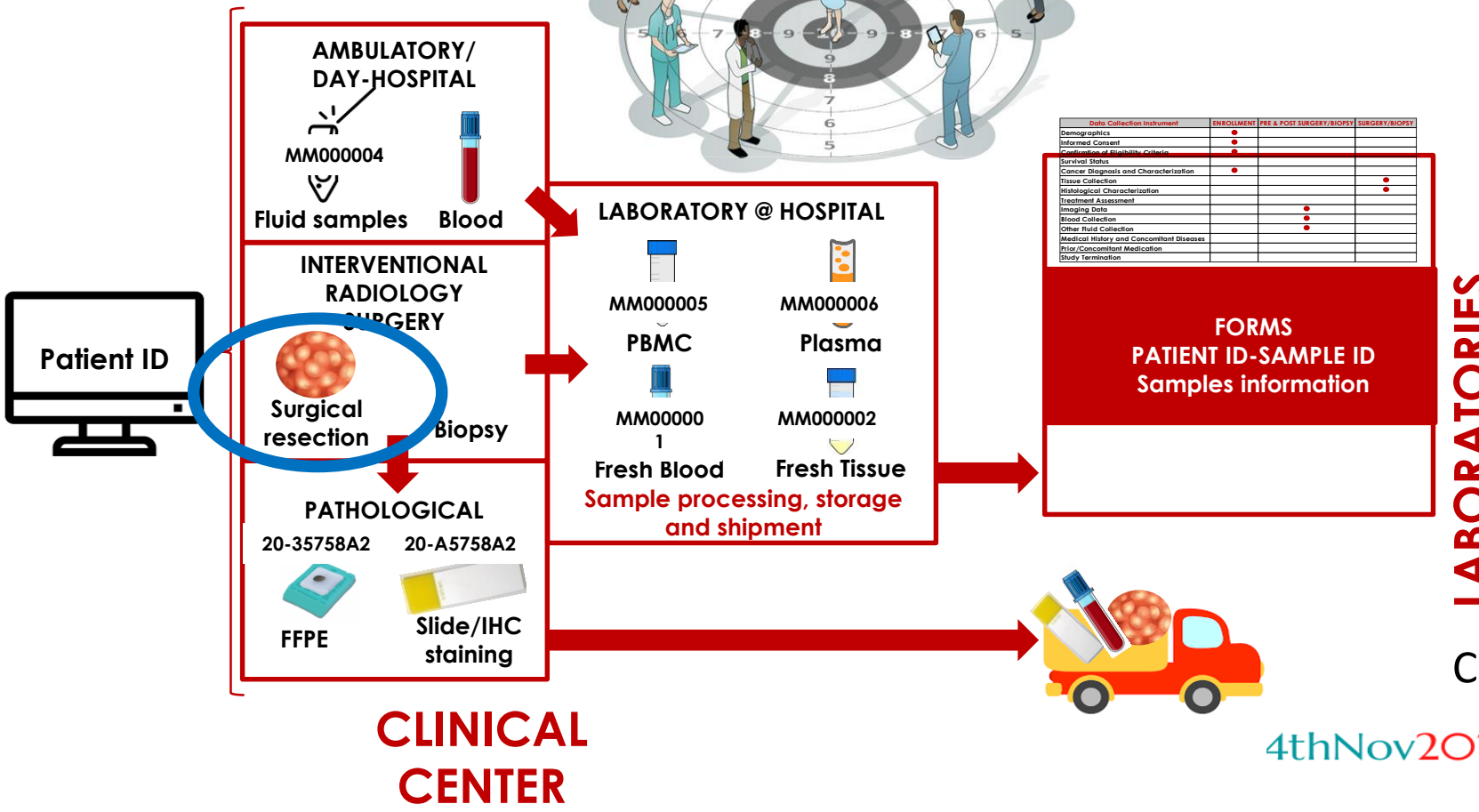
Modern concept of surgical oncology

Logistic Manager



Courtesy of Anna Bagnato

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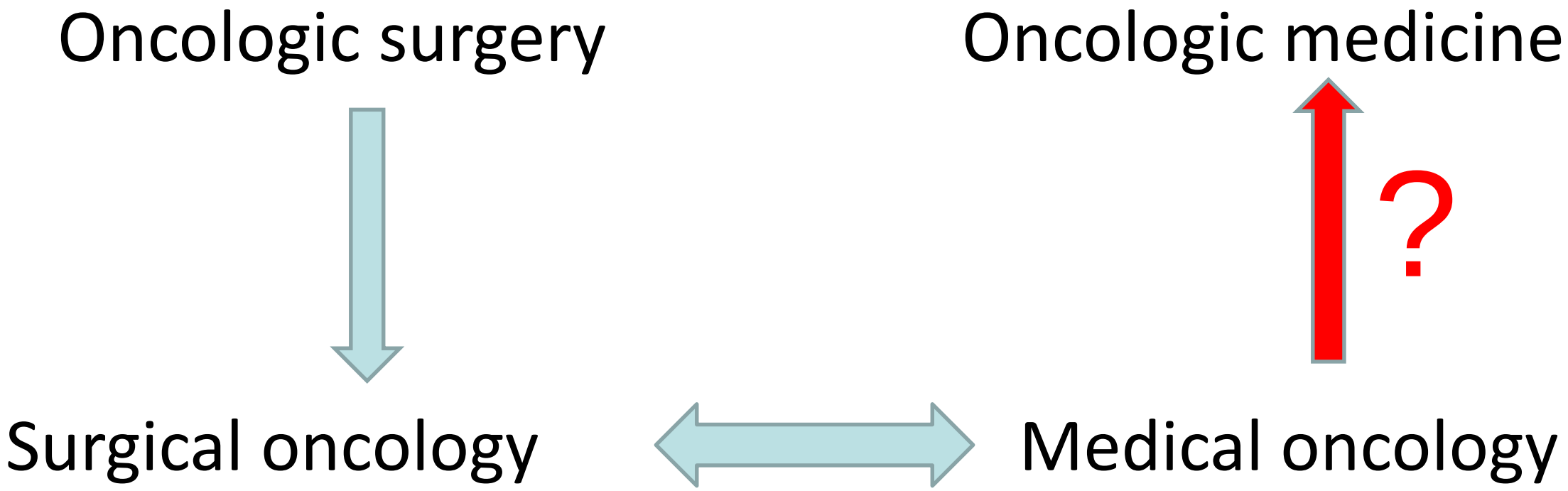
Adding "precision" to surgical treatments



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ORIGINAL ARTICLE

OPEN

Precision Oncology in Surgery

Patient Selection for Operable Pancreatic Cancer

Stephan B. Dreyer, MD,† Mark Pinese, PhD,‡ Nigel B. Jamieson, MD, PhD,*†§ Christopher J. Scarlett, PhD,¶ Emily K. Colvin, PhD,‡ Marina Pajic, PhD,‡ Amber L. Johns, BMedSc,‡ Jeremy L. Humphris, MD, PhD,‡ Jianmin Wu, PhD,‡ Mark J. Cowley, PhD,‡ Angela Chou, MD, PhD,‡‖ Adnan M. Nagrial, MD,‡ Lorraine Chantrill, MD, PhD,‡ Venessa T. Chin, MD, PhD,‡ Marc D. Jones, MPhil,** Kim Moran-Jones, PhD,††, Australian Pancreatic Cancer Genome Initiative,‡, Glasgow Precision Oncology Laboratory,∗, Christopher Ross Carter, MD,† Euan J. Dickson, MD,† Jaswinder S. Samra, MD, DPhil,‡‡§§ Neil D. Merrett, MD,¶¶‖‖ Anthony J. Gill, MD, PhD,‡***††† James G. Kench, MD,‡‡‡‡ Fraser Duthie, MD,*§§§ David K. Miller, BASc,¶¶¶ Susanna Cooke, PhD,* Daniela Aust, MD, PhD,‖‖‖‖ Thomas Knösel, MD,**** Petra Rümmele, MD,†††† Robert Grützmann, MD, PhD,‡‡‡‡ Christian Pilarsky, MD, PhD,‡‡‡‡ Nam Q. Nguyen, MD,§§§§ Elizabeth A. Musgrove, PhD,* Peter J. Bailey, PhD,* Colin J. McKay, MD,*† Andrew V. Biankin, MD, PhD,*† and David K. Chang, MD, PhD*†*

(*Ann Surg* 2020;272:366–376)

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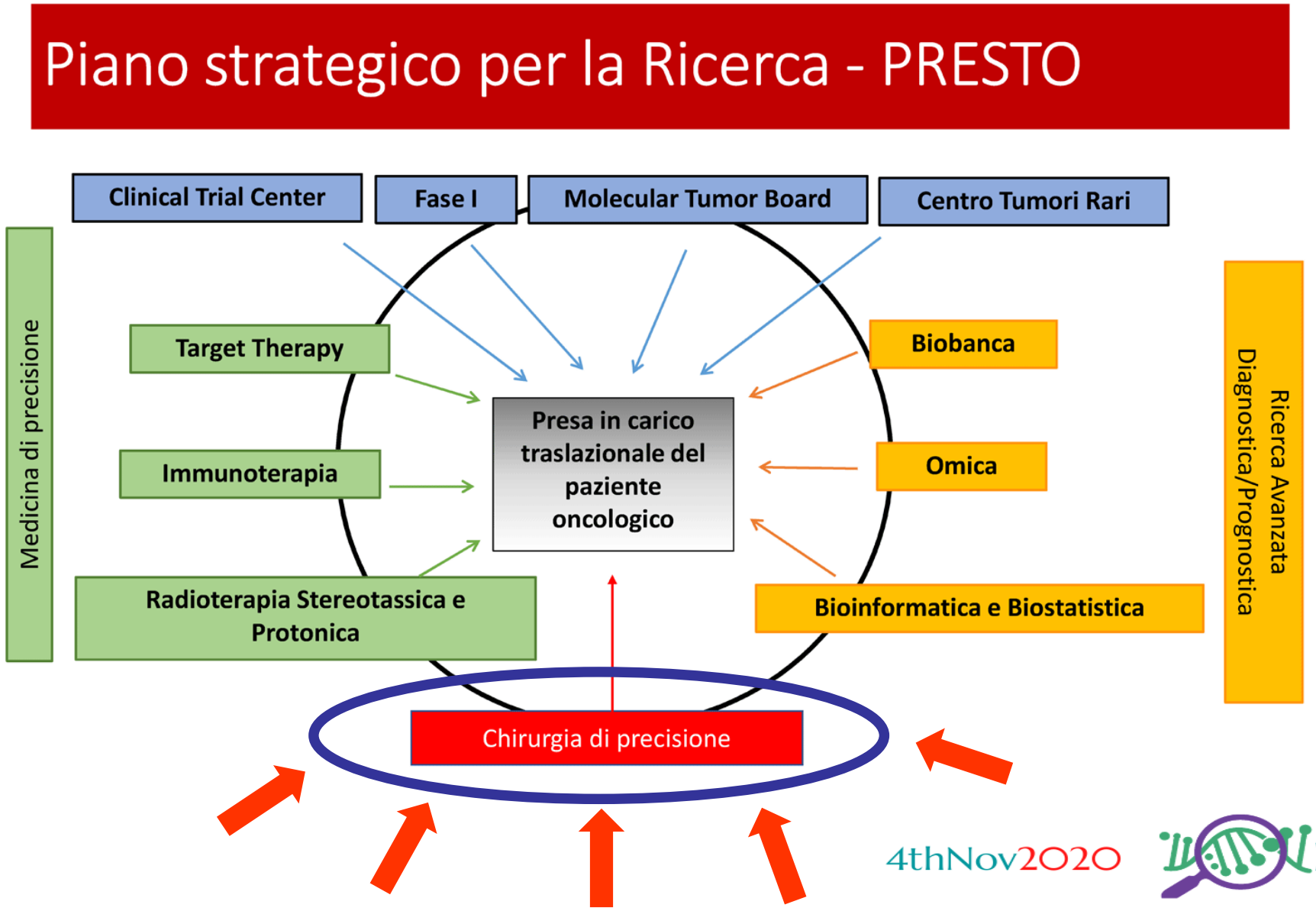

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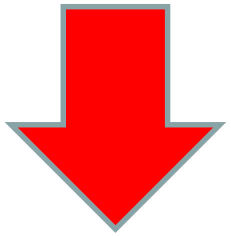
For several cancer diseases,

- surgical resection offers the only chance of cure,
- with chemotherapy adding modest benefit,
- but surgery can be associated with significant morbidity and mortality risk.

Adding "precision" to surgical treatments

In the case of pancreatic cancer, even with complete resection and adjuvant chemotherapy, the 5-year survival rate is only approximately 20%, with approximately 30% succumbing within the first year (mostly due to distant metastatic disease).

Due to this high metastatic recurrence rate, for these patients surgical resection brings uncertain benefit.



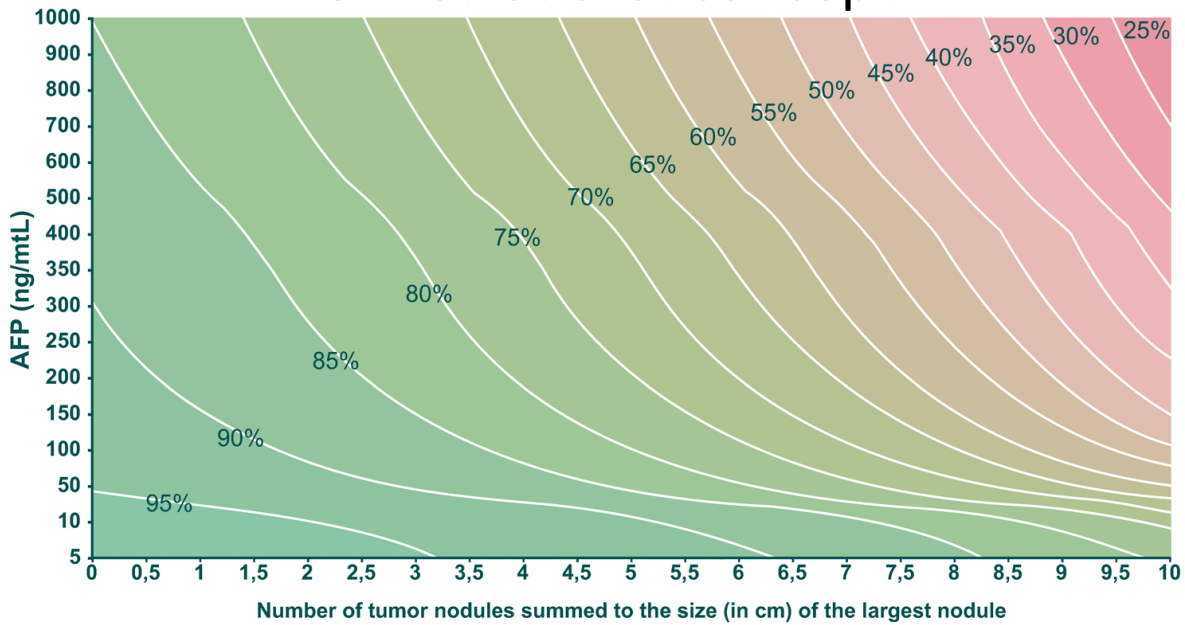
In settings like this, it becomes evident that the high rate of “early” failures indicate current staging modalities for cancers cannot identify patients with occult metastases and aggressive biology.

Biological Markers in Surgery

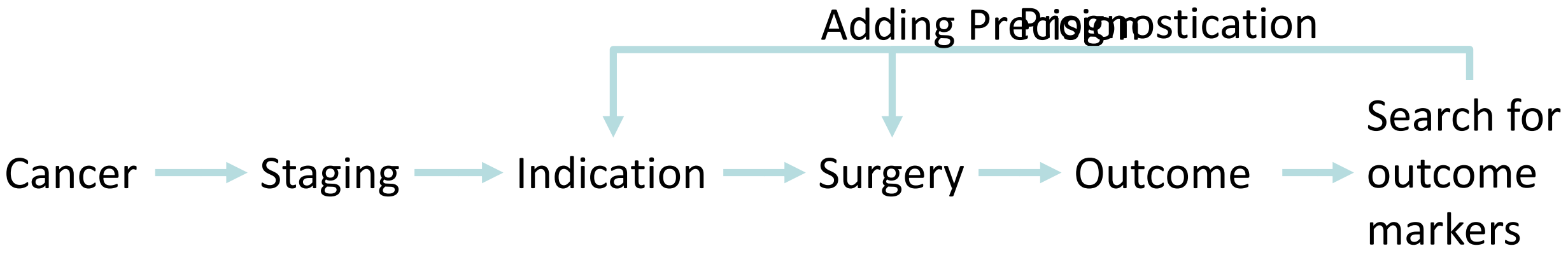
Prognostication

Cancer → Staging → Indication → Surgery → Outcome → Search for outcome markers

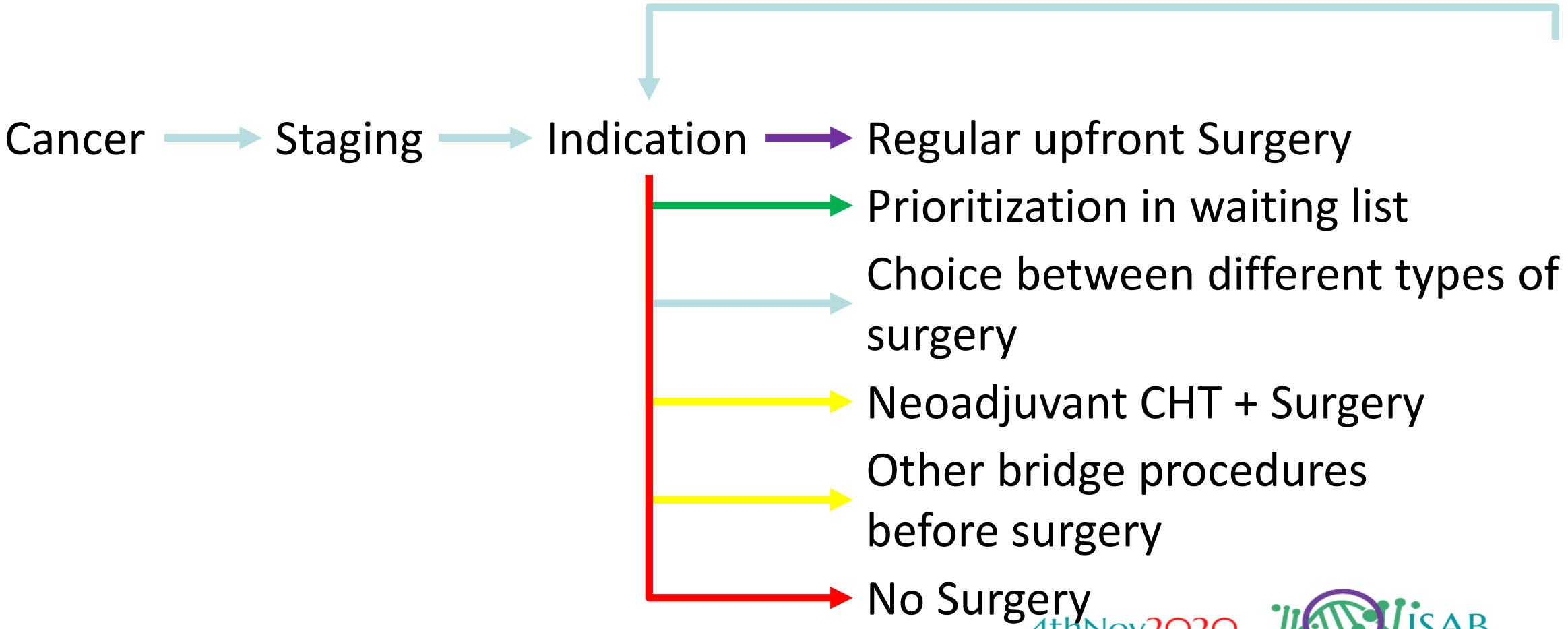
The Metroticket concept



Biological Markers in Surgery



Biological Markers in Surgery

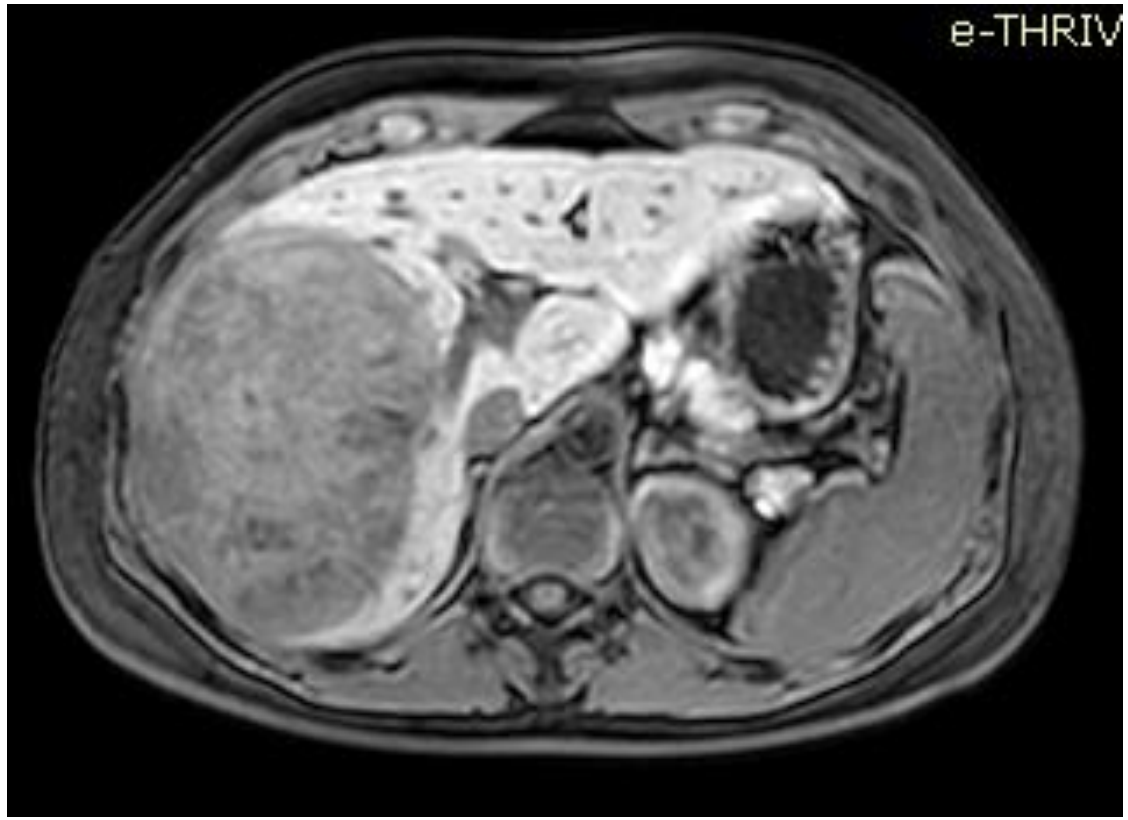


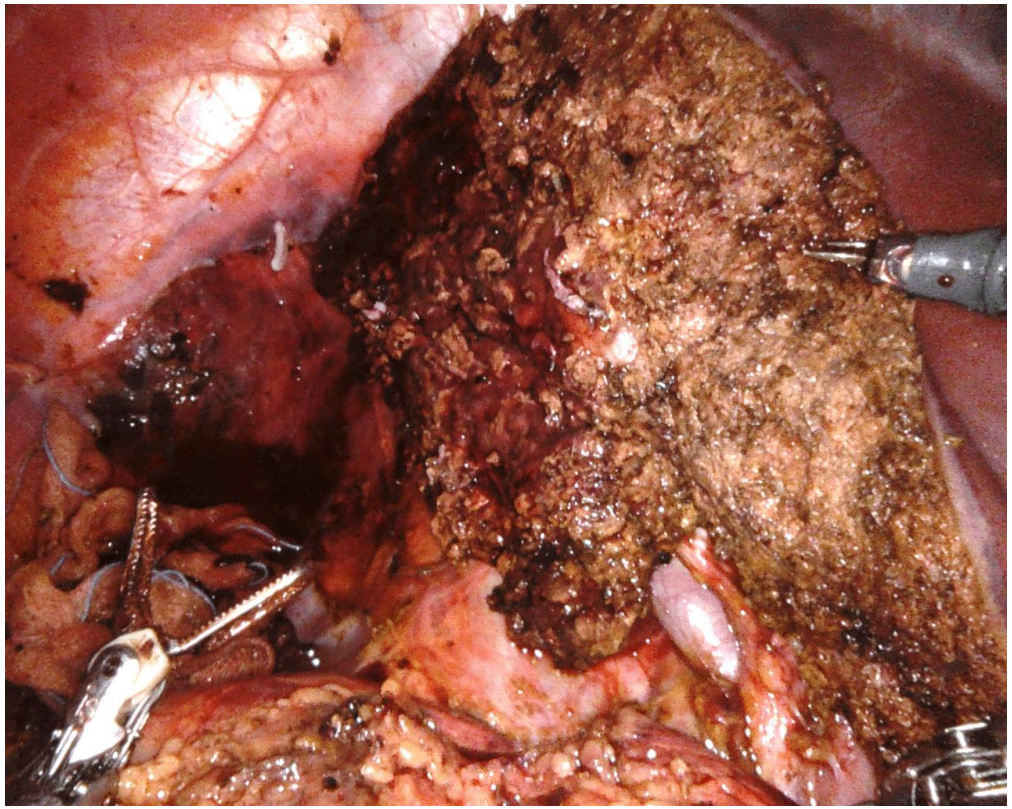
10 Surgical Units at Regina Elena

- Breast Surgery
  (Claudio Botti)
- ENT Surgery
  (Raul Pellini)
- Gynecologic Surgery
  (Enrico Vizza)
- HPB Surgery
  (Gian Luca Grazi)
- Neurosurgery
  (Stefano Telera)
- Orthopaedic Surgery
  (Roberto Biagini)
- Plastic & Recostructive Surgery
  (Roy De Vita)
- Peritoneal Surgery
  (Mario Valle)
- Thoracic Surgery
  (Francesco Facciolo)
- Urologic Surgery
  (Giuseppe Simone)

10 Surgical Units at Regina Elena

1 – Improving precision in technique





Fully robotic bloodless «regolated» Right Hepatectomy

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10 Surgical Units at Regina Elena

2 – Improving precision in surgical care

CONSENSUS STATEMENT

OPEN

Check for updates

Cholangiocarcinoma 2020: the next horizon in mechanisms and management

Jesus M. Banales[1,2,3]✉, Jose J. G. Marin[2,4], Angela Lamarca[5,6], Pedro M. Rodrigues[1], Shahid A. Khan[7], Lewis R. Roberts[8], Vincenzo Cardinale[9], Guido Carpino[10], Jesper B. Andersen[11], Chiara Braconi[12], Diego F. Calvisi[13], Maria J. Perugorria[1,2], Luca Fabris[14,15], Luke Boulter[16], Rocio I. R. Macias[2,4], Eugenio Gaudio[17], Domenico Alvaro[18], Sergio A. Gradilone[19], Mario Strazzabosco[14,15], Marco Marzioni[20], Cédric Coulouarn[21], Laura Fouassier[22], Chiara Raggi[23], Pietro Invernizzi[24], Joachim C. Mertens[25], Anja Moncsek[25], Sumera Rizvi[8], Julie Heimbach[26], Bas Groot Koerkamp[27], Jordi Bruix[2,28], Alejandro Forner[2,28], John Bridgewater[29], Juan W. Valle[5,6] and Gregory J. Gores[8]

NATURE REVIEWS | GASTROENTEROLOGY & HEPATOLOGY VOLUME 17 | SEPTEMBER 2020 | 557

Clinicopathological and molecular features of cholangiocarcinoma

CCA type	Gross pattern	Precancerous lesion	Underlying disease	Tissue markers[a]	Frequent mutations
iCCA — CLC	Mass-forming	None	Viral, cirrhosis	NCAM	*IDH1/2*, *FGFR2* fusions, *BAP1*, *BRAF*, *ARID1A*, *KRAS*, *TP53*, *SMAD4* Increased *IDH1* and *TP53*
iCCA — small duct type	Mass-forming	None	Viral, cirrhosis	NCAM, N-cadherin, SMAD4, BAP1^{loss}	*IDH1/2*, *FGFR2* fusions, *BAP1*, *BRAF*, *ARID1A*, *KRAS*, *TP53*, *SMAD4* Increased *IDH1/2*, *FGFR2* fusion
iCCA — large duct type	Periductal infiltrating (±mass-forming) or intraductal growing	Biliary epithelial neoplasia, IPNB, ITPN, mucinous cystic neoplasm	Primary sclerosing cholangitis, liver flukes	Mucin[b], MUC5AC, MUC6, S100P, SMAD4^{loss}, BAP1	*IDH1/2*, *FGFR2* fusions, *BAP1*, *BRAF*, *ARID1A*, *KRAS*, *TP53*, *SMAD4* Increased *KRAS* and *TP53*
pCCA–dCCA	Periductal infiltrating or intraductal growing	Biliary epithelial neoplasia, IPNB, ITPN, mucinous cystic neoplasm	Primary sclerosing cholangitis, liver flukes	Mucin[b], MUC5AC, MUC6, S100P, SMAD4^{loss}, BAP1	*KRAS*, *TP53*, *SMAD4*, *ERBB3*, *PRKACA–PRKACB* fusions, *ELF3*

CCA, cholangiocarcinoma; CLC, cholangiolocarcinoma; dCCA, distal cholangiocarcinoma; iCCA, intrahepatic cholangiocarcinoma; IPNB, intraductal papillary neoplasm of the bile duct; ITPN, intraductal tubulopapillary neoplasm; pCCA, perihilar cholangiocarcinoma. [a]Markers from single-centre experience; international criteria and consensus on a definite panel of markers are still needed. [b]Mucin refers to histomorphological stains periodic acid–Schiff (PAS) or Alcian PAS.

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10 Surgical Units at Regina Elena

2 – Improving precision in surgical care

Surgical Units

Researchers

Translationality

- DMT
- Molecular Board
- Other institutional setting?

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Active or Planned Research Protocols in Surgery

UOC - UOSD	Progetto
HPB Surgery	Surgery guided by genetic mutation
Gynecology	• BRCA and genetic profile in ovarian cancer • Circulant DNA and NETosi • Cryoconservation of ovarian tissue and germinal cells • Robotic Surgery • “Single-site” surgery
Peritoneal Surgery	• Pharmacogenetic in the personalization of HIPEC • Nanoparticles • Mesothelioma carcinosis • Ovarian cancer carcinosis
ENT Surgery	MicroRNA expression profiles
Orthopedic Surgery	Computer Assisted Orthopaedic Surgery (CAOS)
Breast Surgery	• Identification of intermediate biopathological markers for preventive purposes • Identification of new imaging techniques for diagnosis and treatment of subclinical lesions • Volume-replacement conservative oncoplasty
Urologic Surgery	Magnification of the robotic surgical field

Adding "precision" to surgical treatments

Future vision of surgical research (any field)

UOC - UOSD	
HPB Surgery	Implementation of the study of the single genetic profile of the patient before surgery
Gynecology	• Genetic/biomolecular indicators that help personalize the surgery/chemotherapy integration. • Identification of a biomarker for the risk of reintroduction of tumor cells in ovarian tissue transplantation
Peritoneal Surgery	• The definition of the indication for treatment with cytoreduction and HIPEC of colon carcinosis in mutated k-ras • PCI in gastric cancer, • the evaluation of the stroma/mucus ratio in carcinosis of the digestive tract of mucinous origin, • the differentiation between low and high grade appendix tumors with different treatment procedures.
Orthopedic Surgery	• Development/improvement of navigation systems for complex surgical procedures on three-dimensionally complex anatomical areas such as spine and pelvis; • Realization of ad-hoc surgical instruments to achieve minimum invasiveness and maximum surgical accuracy; • Development of customized composite prosthetic implants, based on bioengineered structures, in order to achieve an anatomically exact reconstruction and maximum biomechanical and biological compatibility; • Production of templates for custom-made cemented spacers for use in revision surgery
Neurosurgery	• Implement surgical treatments for resection of primary and secondary brain tumors with both morphological and functional image guidance • Implement the use of the 5-ALA drug as a fluorescence-guided imaging system • Implementation and standardization of neurophysiological monitoring techniques for the removal of brain lesions in critical locations
Breast Surgery	• Identification of tumor risk molecular signatures • Definition of new therapeutic standards for the treatment of non-palpable lesions. • Standardization of innovative conservative surgical techniques.
Urologic Surgery	• Standardize robotic surgery also in the oligometastatic patient • To establish if they exist and what are the advantages of robotic surgery in the treatment of musculoskeletal neoplasia of the bladder.

Round Table #2

Precision Surgery

From 3 pm to 4.30 pm

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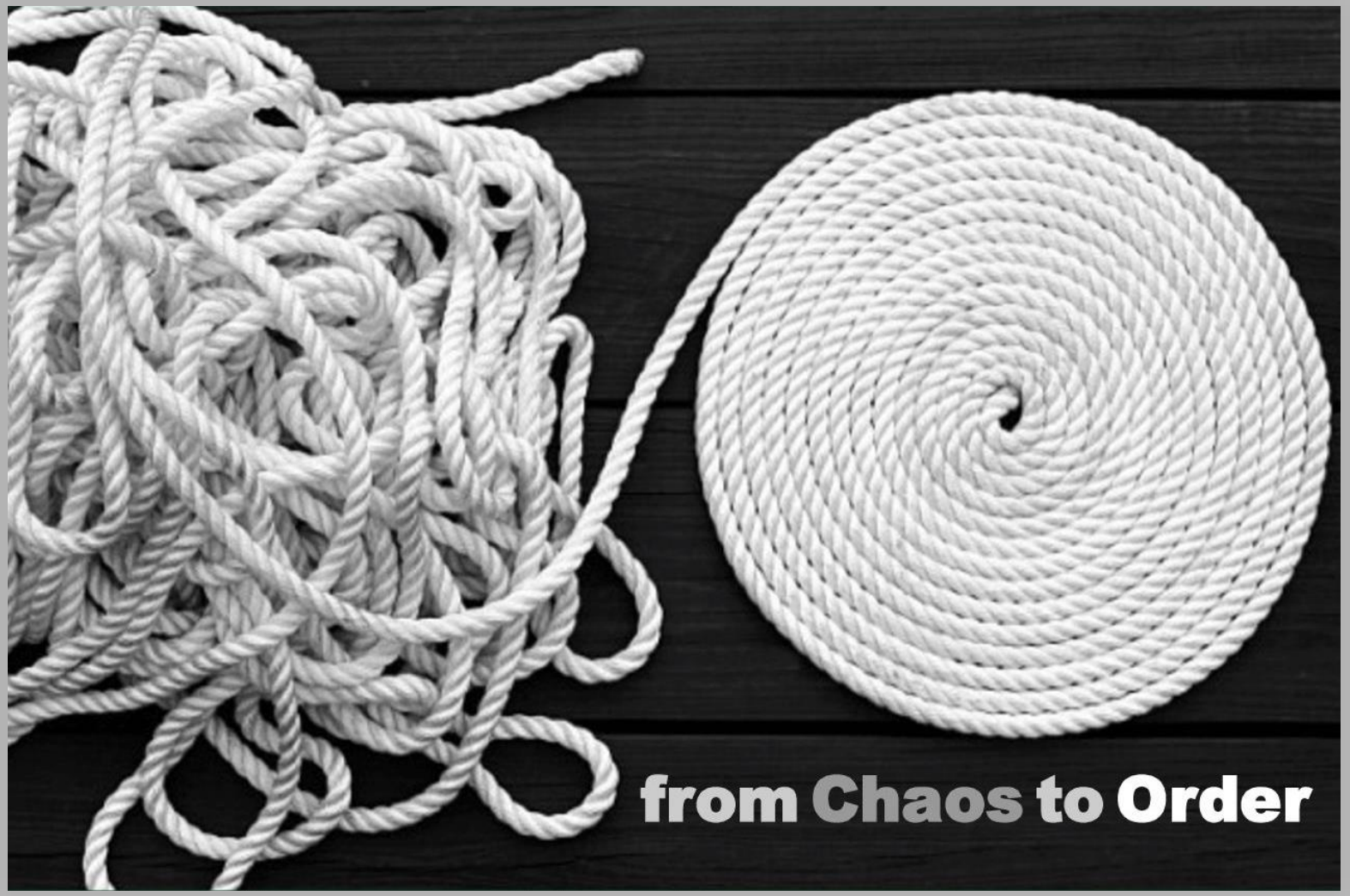

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