

■ Multidisciplinary care for Colorectal Cancer

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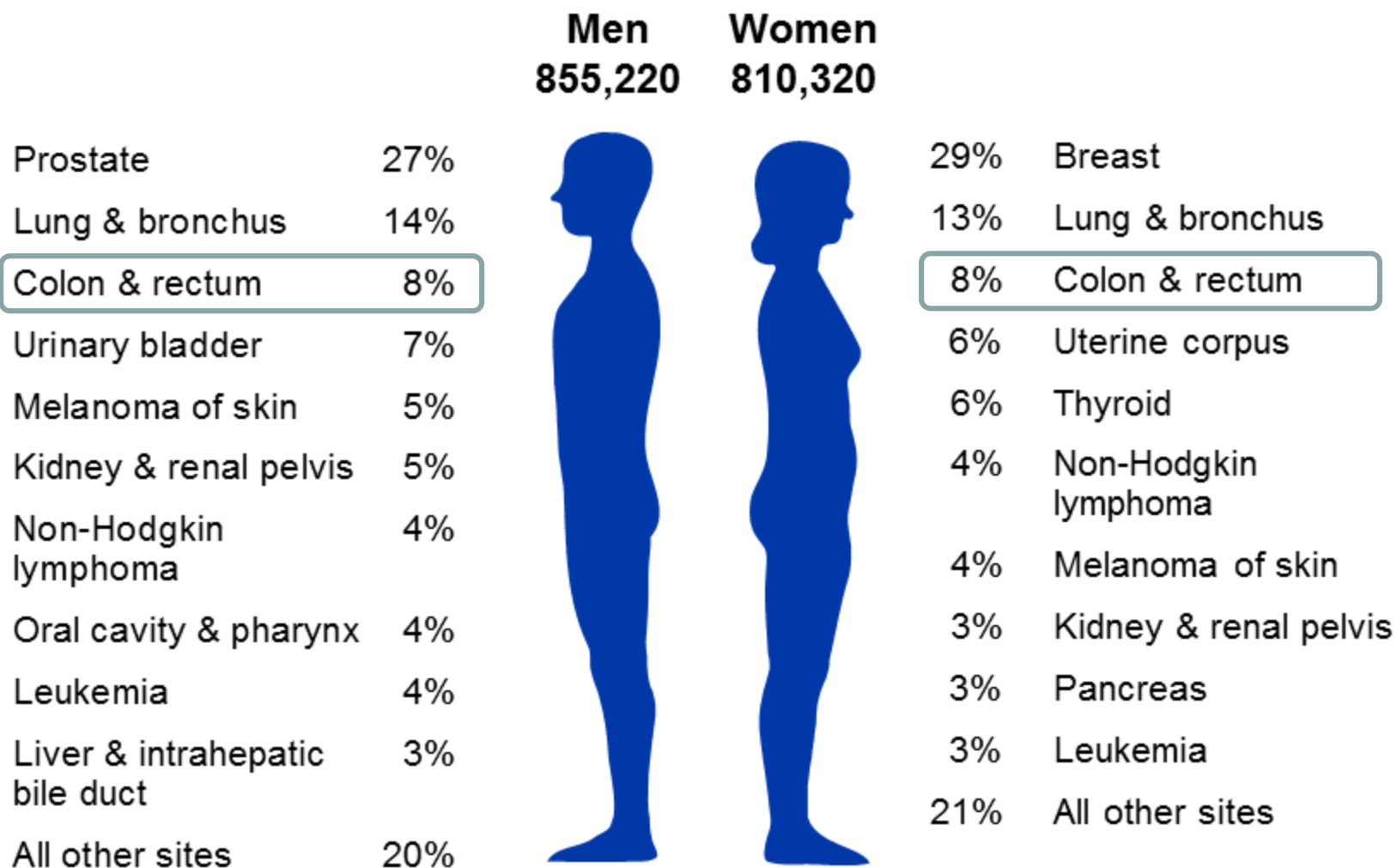


■ Disclosures

- No Disclosures

- **Facts and Figures**
- **Risk Factors, screening**
- **Clinical Presentation and Management**
- **Multidisciplinary care**
- **MDC of colon cancer metastasized to the liver**

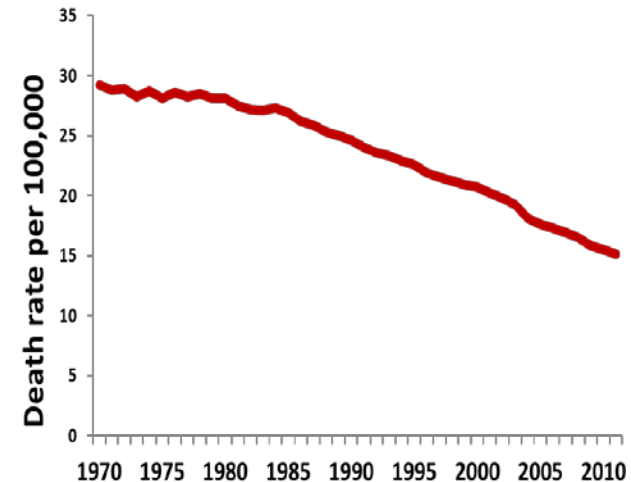
Estimated New Cancer Cases* in the US in 2014



*Excludes basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder.

Colorectal Cancer Mortality

- Decline due to:
 - Improvements in treatment
 - **Screening** → earlier detection
 - **Screening** → prevention



- It is estimated that screening has prevented more than **500,000** colorectal cancers in the US over the past three decades; **but other factors contribute as well**



Risk Factors

- Adenomatous polyps
- Age
- Inflammatory Bowel Disease
- History of Cancer
- Family History of Colorectal Cancer
- Physical Inactivity/obesity
- Smoking
- Diets/Supplements
- Race

■ Non-Modifiable Risk Factors



AGE

- 90% of cases occur in people 50 and older



GENDER

- Slight male predominance, but common in both men and women



Race/Ethnicity – higher rates among

- African Americans
- Native Americans (esp. Northern Plains Tribes)
- Alaska Natives
- Ashkenazi Jews

■ Modifiable Risk Factors

Lack of Physical Activity

Less Active → Raises risk

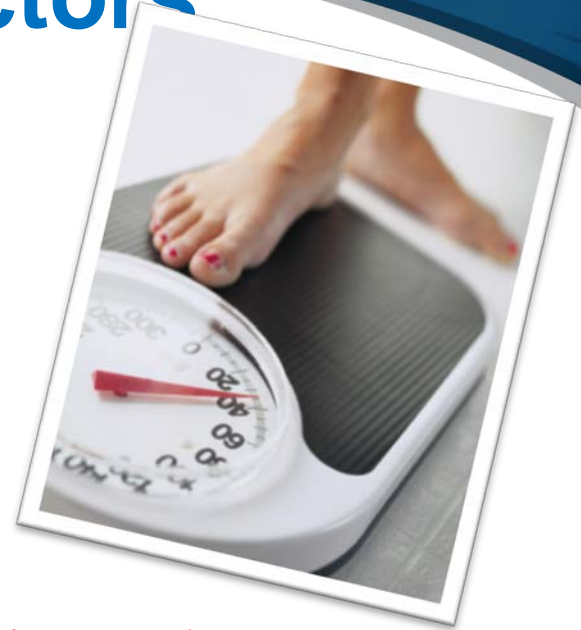
Overweight

Obesity → Raises risk of having and of dying from CRC

Smoking → Raises risk

Alcohol use → Raises risk

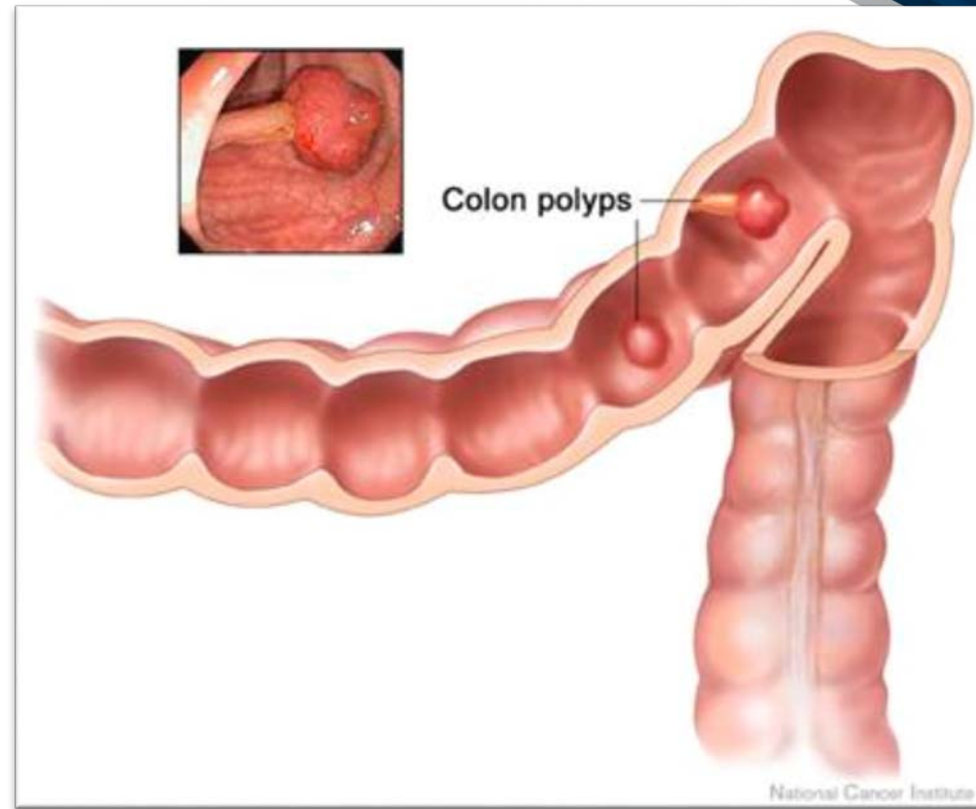
Type 2 diabetes → Raises risk



■ Risk Factor - Polyps

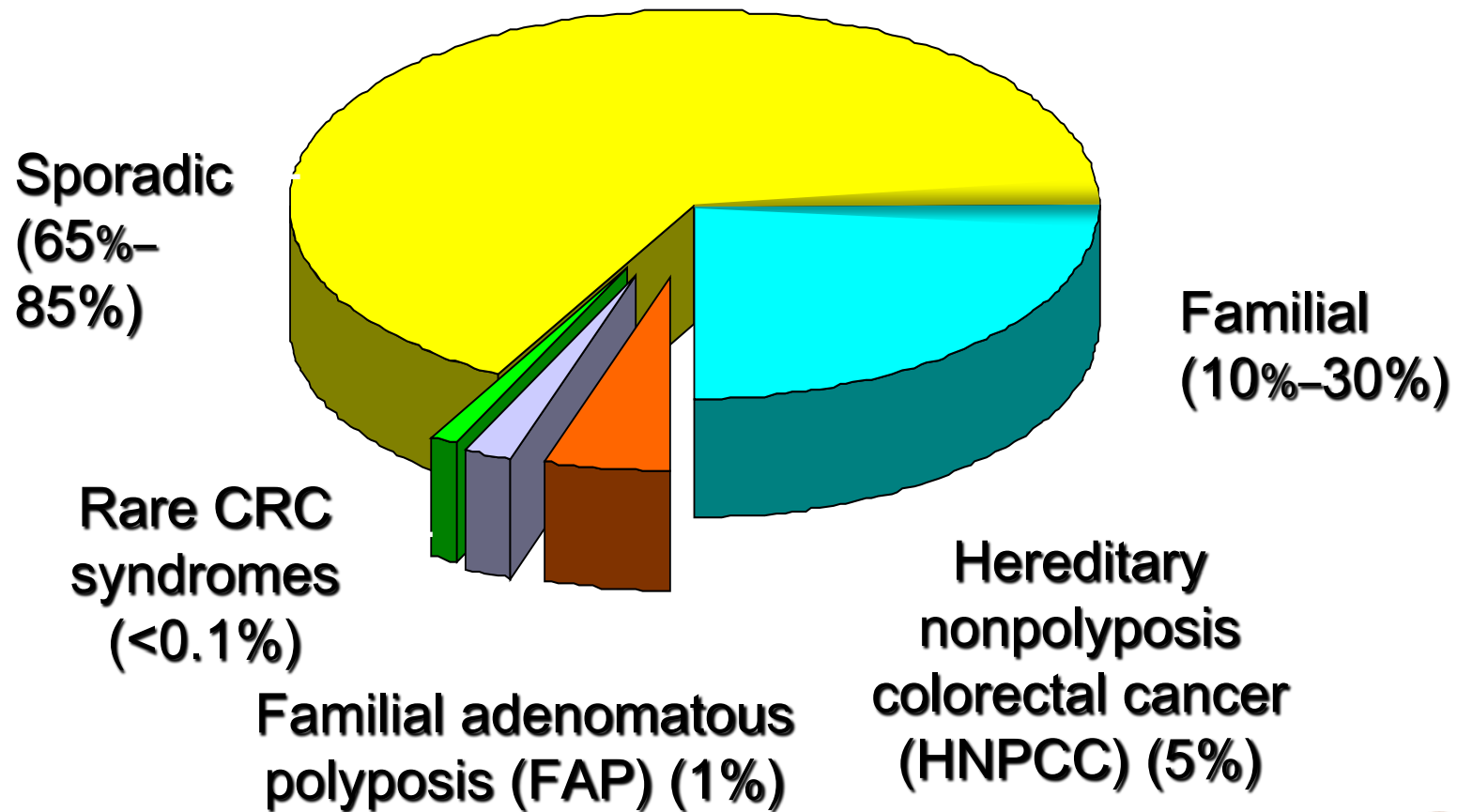
Different types of polyps:

- Hyperplastic
 - Low risk: very small chance they'll grow into cancer
- Adenomatous
 - About **9 out of 10** colon and rectal cancers start as adenomas



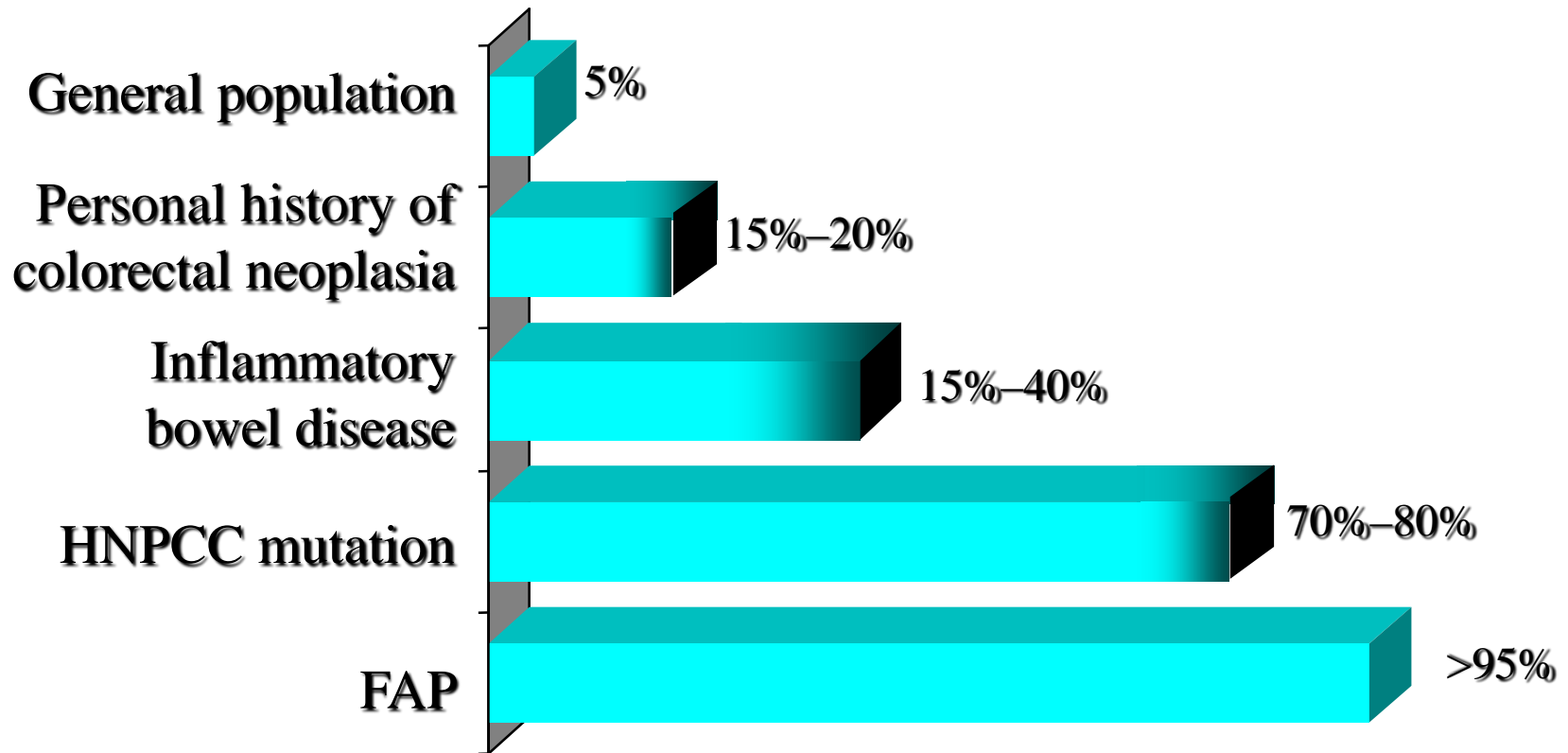
It may take ≥ 10 -15 years for polyps to become cancer

■ Risk Factors- genetics



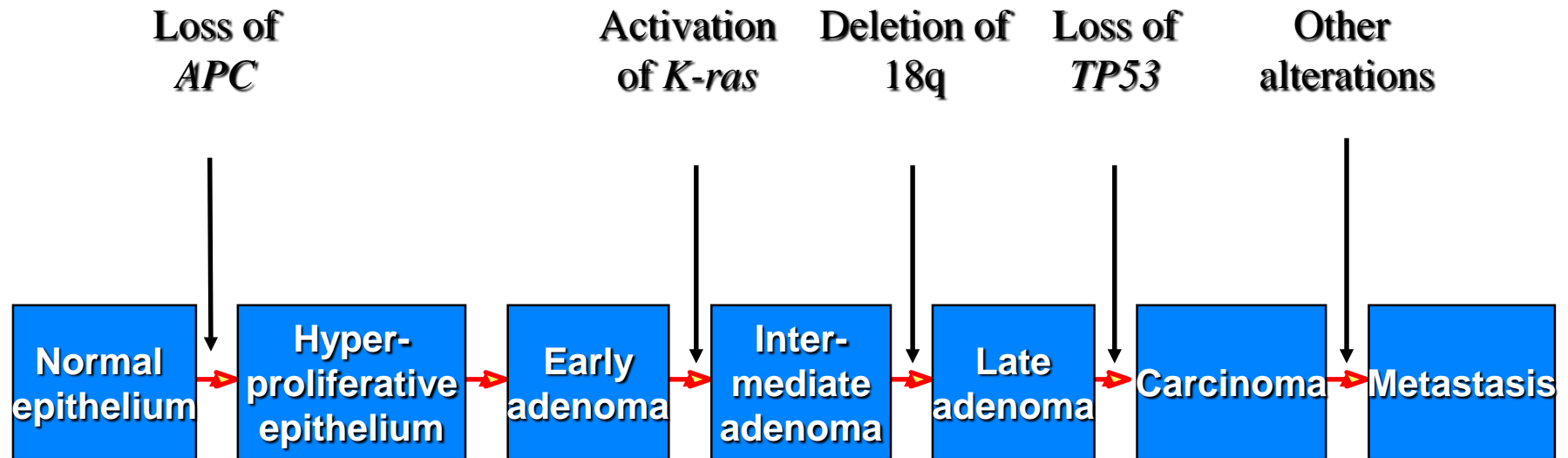
Adapted from Burt RW et al. *Prevention and Early Detection of CRC*, 1996

Risk of Colorectal Cancer



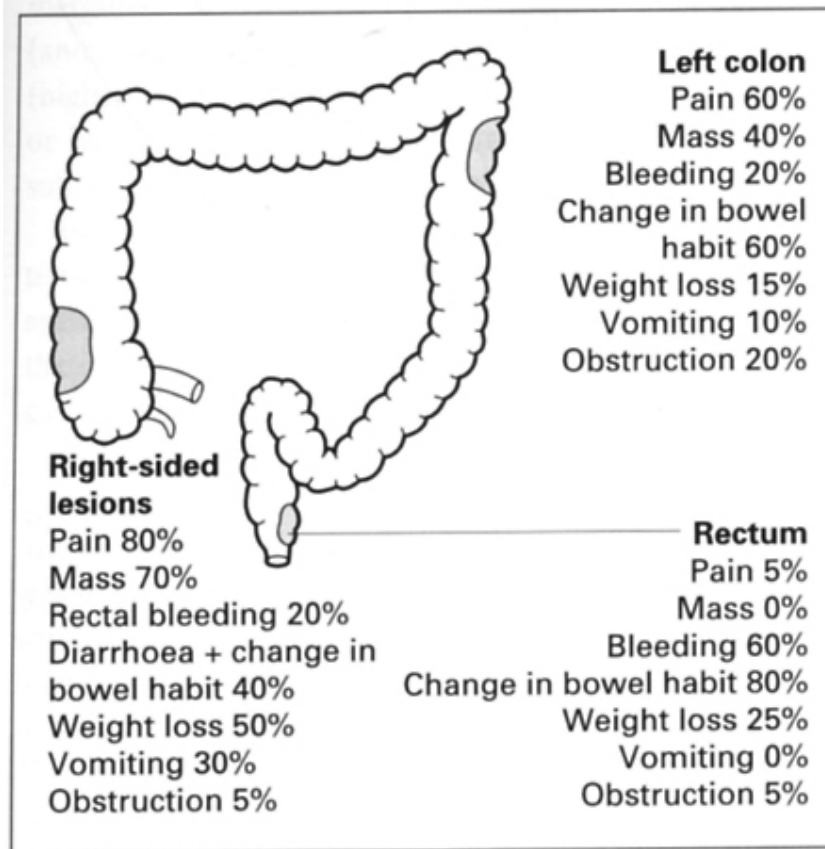
Lifetime risk (%)

Adenoma-Cancer Sequence



Adapted from Fearon ER. *Cell* 61:759, 1990

Clinical Presentation



Cancer of the colon as seen on barium enema

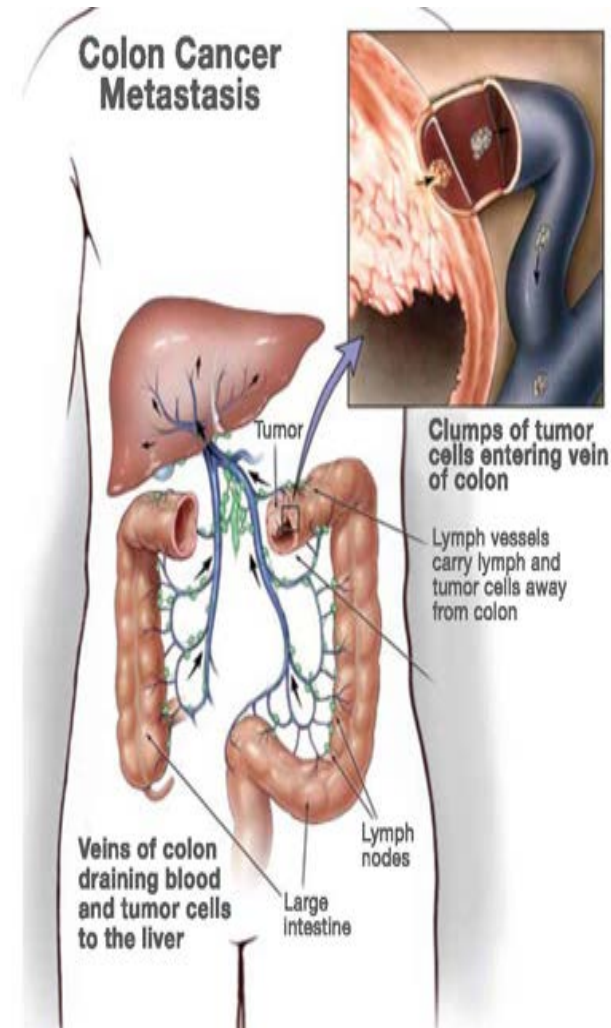
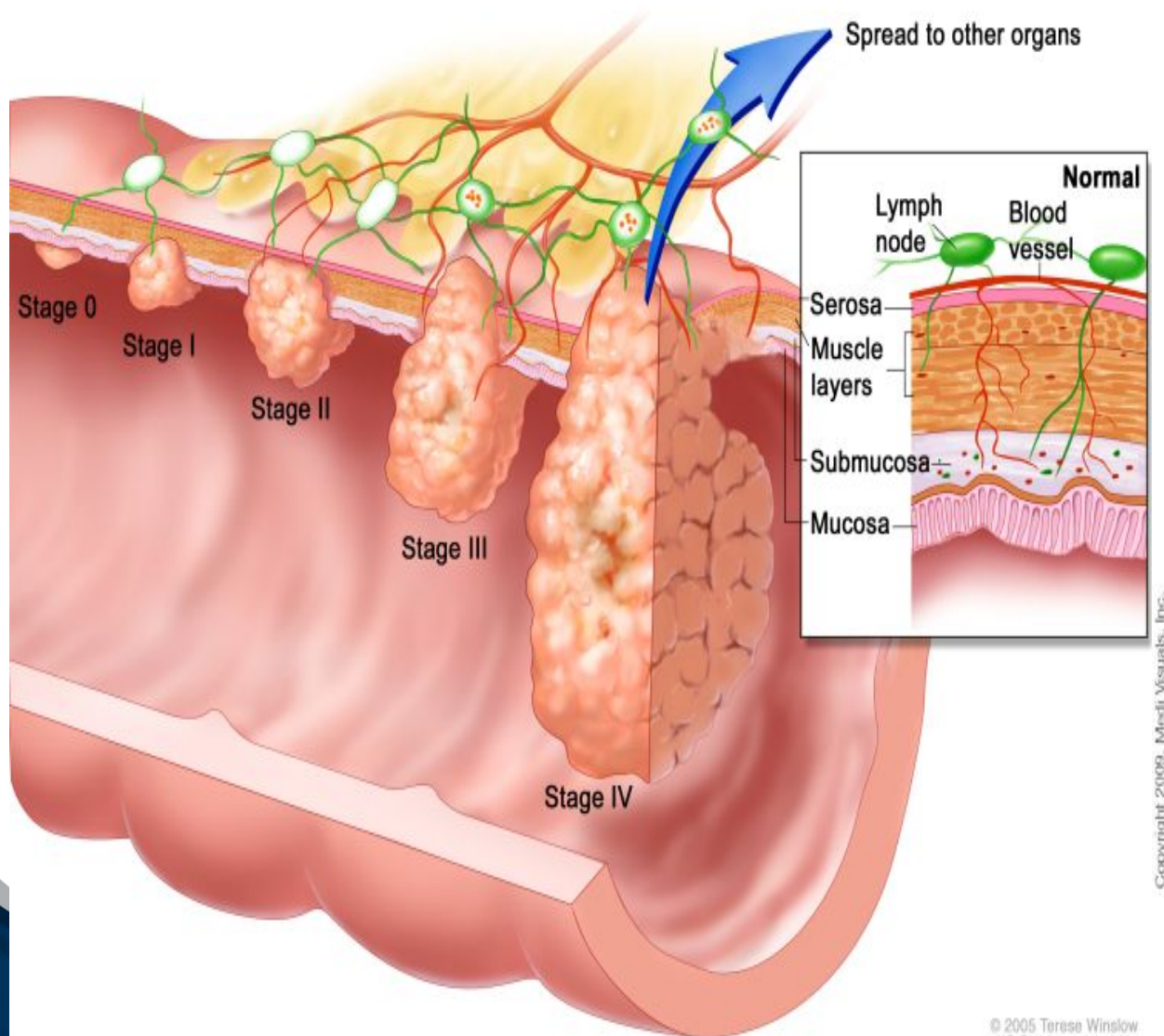


Double contrast barium enema shows an apple-core lesion surrounding the lumen of the descending colon.

Courtesy of Jonathan Kruskal, MD.

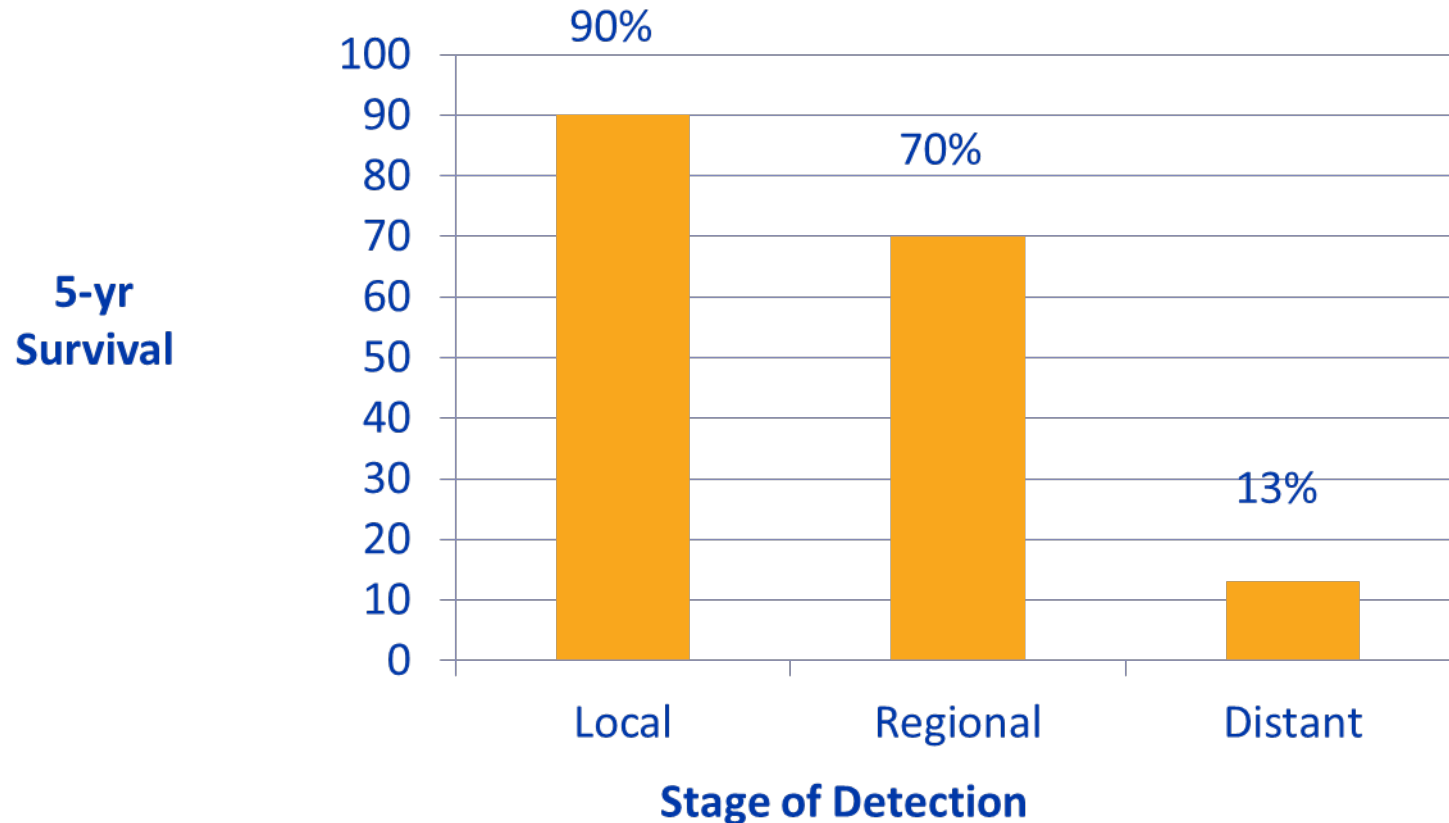
Graphic 75818 Version 3.0

STAGES OF COLON CANCER



Benefits of Screening

Survival Rates by Disease Stage*



**only 39% diagnosed at
localized-stage disease**

Recommended Screening Tests

ACS and USPSTF

- Colonoscopy- q 10 yrs
- High Sensitivity Fecal Occult Blood Testing- q1yr
 - Guaiac- FOBT
 - Immunochemical-FIT
- Flexible Sigmoidoscopy (FSIG) -5 yrs
 - Recent studies support efficacy
 - Very limited utilization/availability in U.S.



Screening

- Average Risk
 - Start at age 50
- Family History
 - Start at age 40 or
 - 10 years earlier than youngest family member with cancer
- High Risk
 - Based on risk factors
 - Familial Adenomatous Polyposis; start at age 10-12y and yearly
 - Lynch Syndrome; start at age 20y and q2y till 45y then yearly

Principles of Management

- Surgery is the mainstay of treatment
- Complete removal of tumor with negative margins
- Removal of involved node-bearing tissue
- Avoid spillage or disruption of tumor
- Assess for evidence of metastasis
- Personalized treatment based on molecular profiling

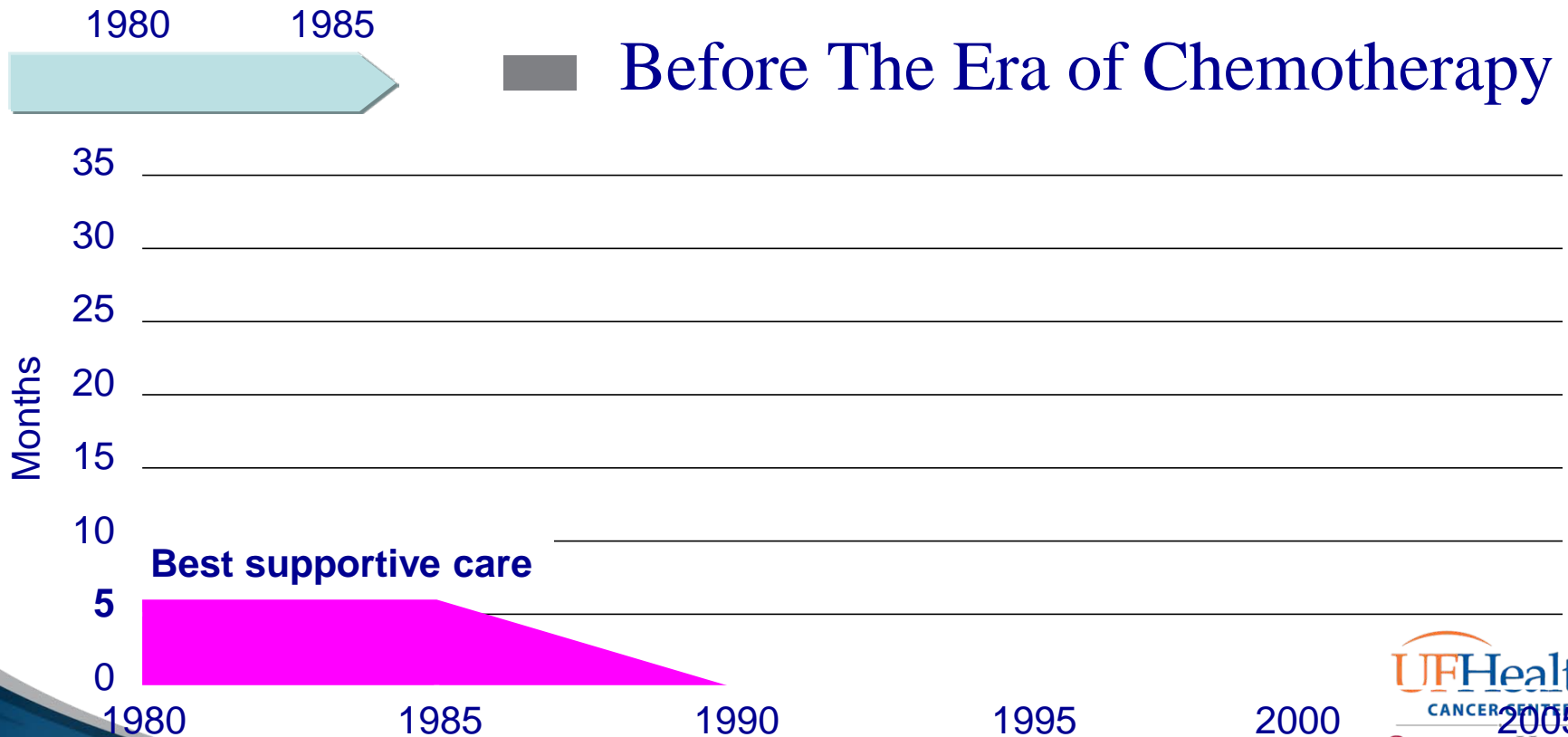
Management

Colon Cancer

- Stage I
 - Surgery alone
- Stage II
 - Surgery alone +/- chemotherapy
- Stage III
 - Surgery + Chemotherapy
- Stage IV
 - Chemotherapy alone
 - Surgery + chemotherapy + metastasectomy

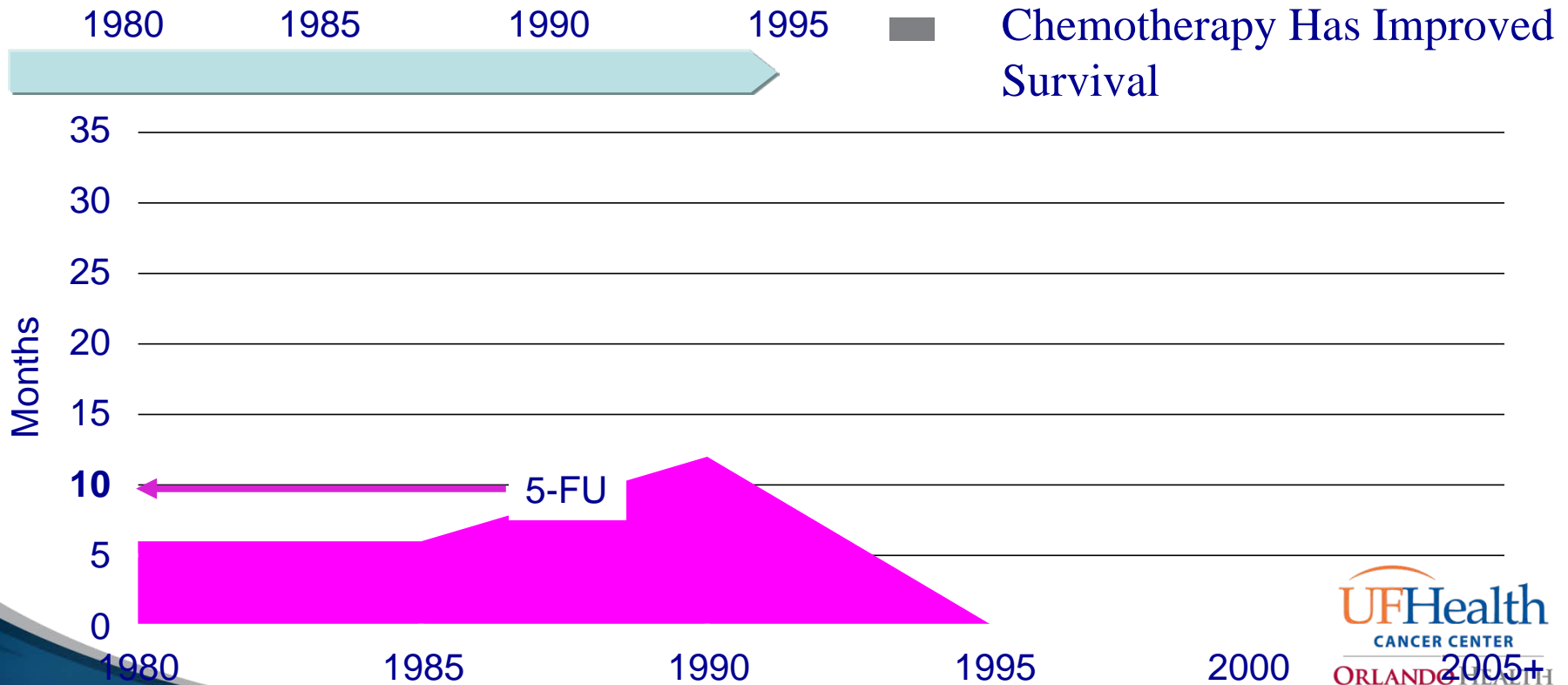
Stage IV disease

- Diagnosis & treatment of CRC - rapidly developed in the past 10-15 years

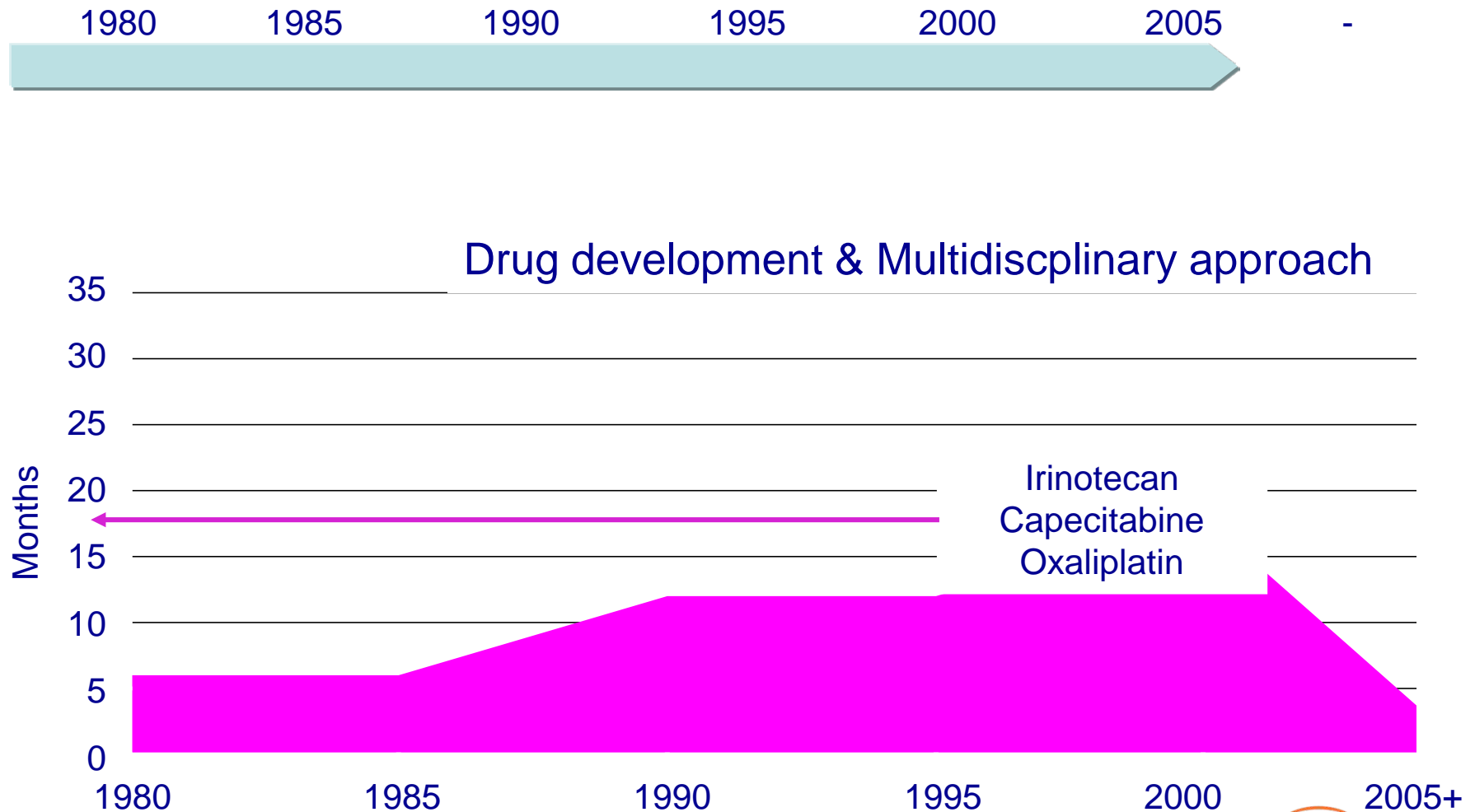


Stage IV

- Diagnosis & treatment of CRC - rapidly developed past 10-15 years
- Managing through a single treatment is difficult.



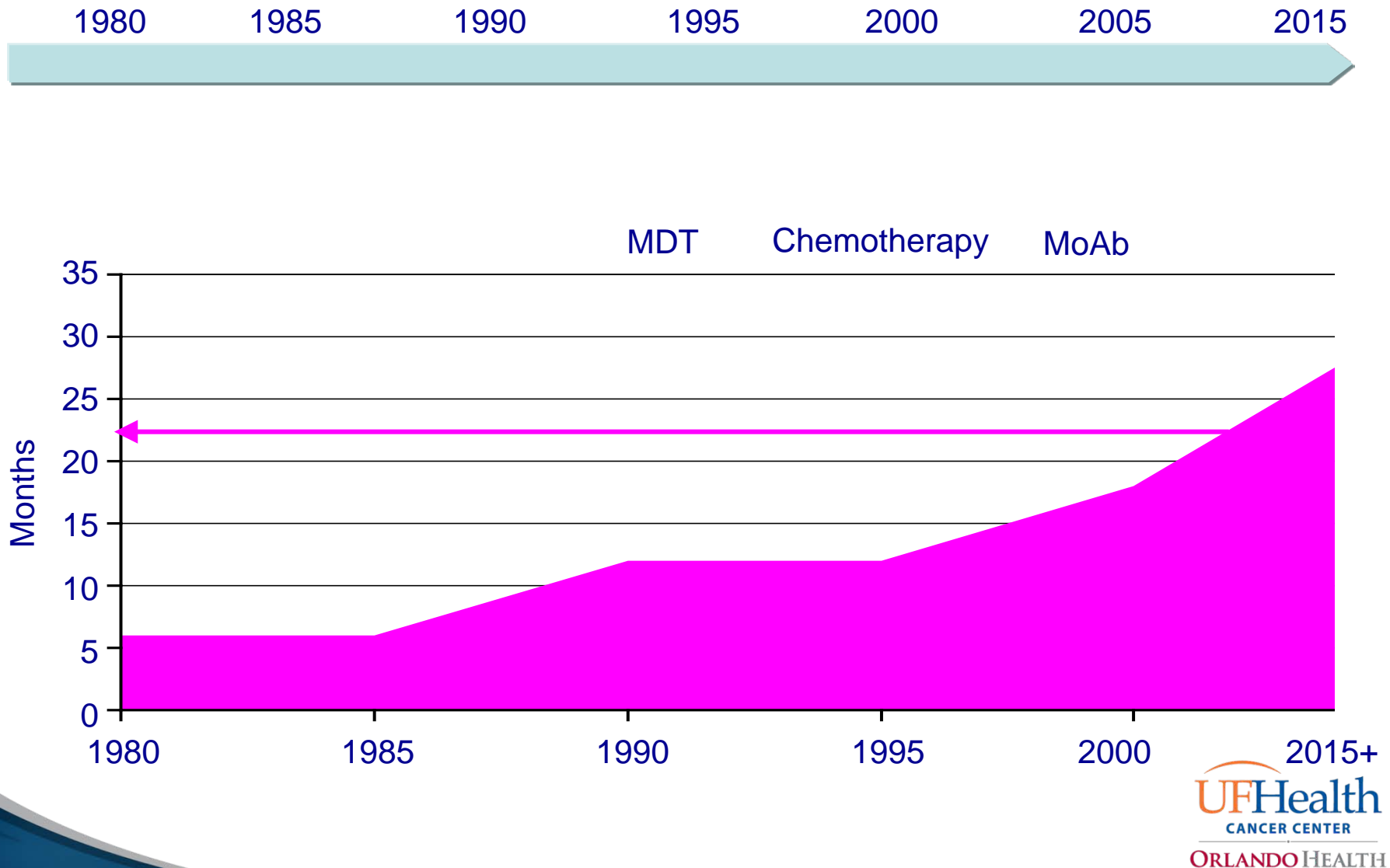
Improved CRC Survival But More To Be Done



mCRC = metastatic colorectal cancer; 5-FU = 5-fluorouracil; MoAbs = monoclonal antibodies;
OS = overall survival

Targeted Therapy Improved CRC Survival

Bevacizumab, Cetuximab, Panitumumab, Afibercept, etc...



Colon cancer MDC



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CLINICAL PRESENTATION

WORKUP^b

FINDINGS

Suspected or
proven metastatic
synchronous
adenocarcinoma
(Any T, any N, M1)

- Colonoscopy
- Chest/abdominal/pelvic CT
- CBC, chemistry profile
- CEA
- Determination of tumor gene status for *RAS* and *BRAF* (individually or as part of next-generation sequencing [NGS panel])^e
- Determination of tumor MMR or MSI status (if not previously done)
- Biopsy, if clinically indicated
- Consider PET/CT scan (skull base to mid-thigh) if potentially surgically curable M1 disease in selected cases
- Multidisciplinary team evaluation, including a surgeon experienced in the resection of hepatobiliary and lung metastases

Synchronous
liver only and/or
lung only
metastases

Resectable^g

Unresectable
(potentially
convertible^g or
unconvertible)

Synchronous
abdominal/peritoneal
metastases

Synchronous
unresectable
metastases of
other sites^t

Definition of MDT (Multidisciplinary team)

- Group of people of different healthcare disciplines who meets together at a given time whether physically in one place, or by video or teleconferencing to discuss a given case who are each able to contribute independently to the diagnostic and treatment decisions about the case.
- Through regular meetings and discussions within MDTs, healthcare professionals can improve communication, cooperation, and decision-making regarding cancer treatment
- The composition of an MDT may vary depending on the cancer type



Oncological Surgeon
Medical Oncologist

Pathologist &
Radiologist

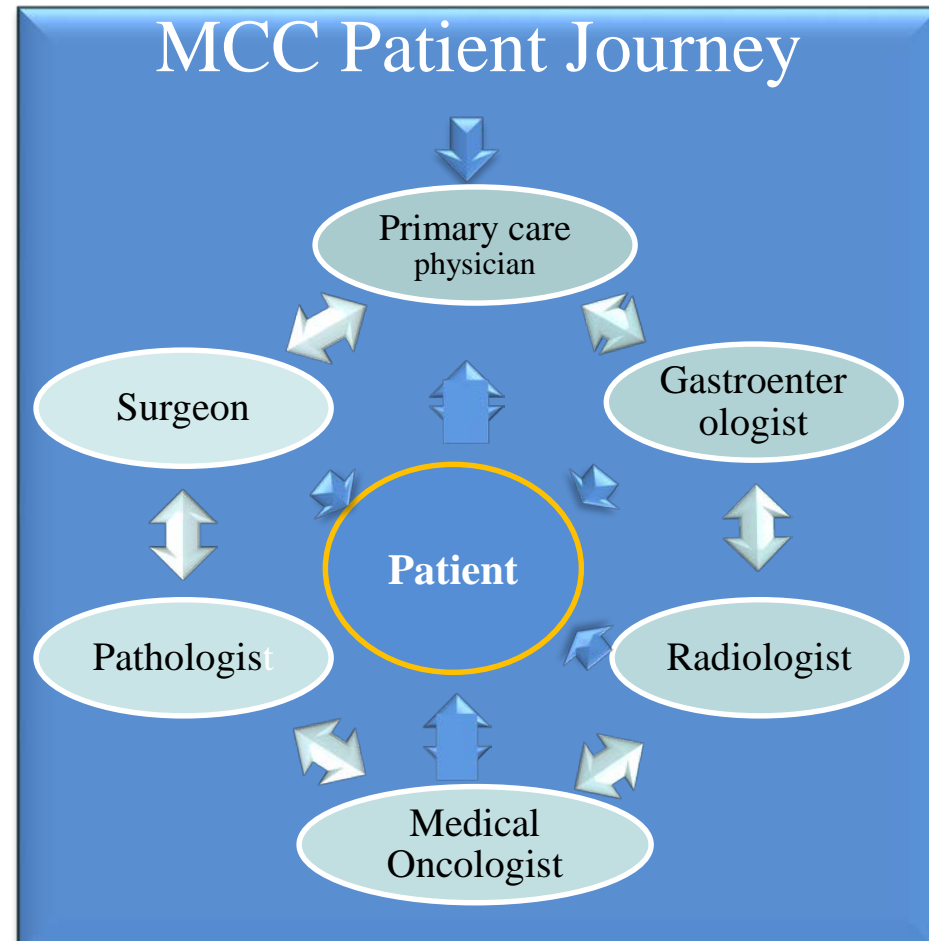
Radio-Oncologist
& Palliative Sp

Gastroenterologist, Nurse practitioner, Nutritionist, Pharmacist, Patient
Navigator

MDTs in cancer care

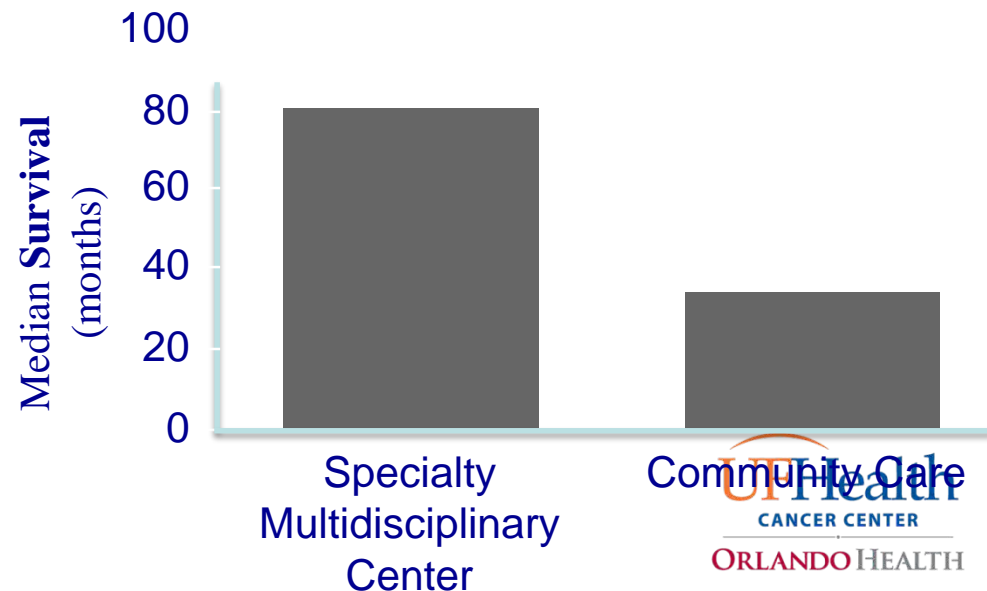
- The cancer-specific outcome is considered more favorable when patients are managed under MDT care

MDTs Improve Patient Outcomes by Combining Specialist Knowledge to Identify Individual Diagnostic & Treatment Options



MDTs in cancer care

- The cancer-specific outcome is considered more favorable when patients are managed under MDT care.
- MDTs can improve clinical decision-making, outcomes & experiences of patients with colorectal cancers.



Outcomes

- Pathology - quality of reports improved, # LN examined in MDT group, more likely to perform MSI testing.
- More complete preop evaluations, and higher rates of access to multimodality therapies.
- Differences - observed in the rates of
 - Chest CT (95.0% vs. 37.1%, $p < 0.001$)
 - CEA (100% vs. 63.8%, $p < 0.001$)
 - Transrectal US for rectal cancer (88.0% vs. 37.7%, $p < 0.001$).

■ The OSTRiCh Consortium (Optimizing the Surgical Treatment of Rectal Cancer)

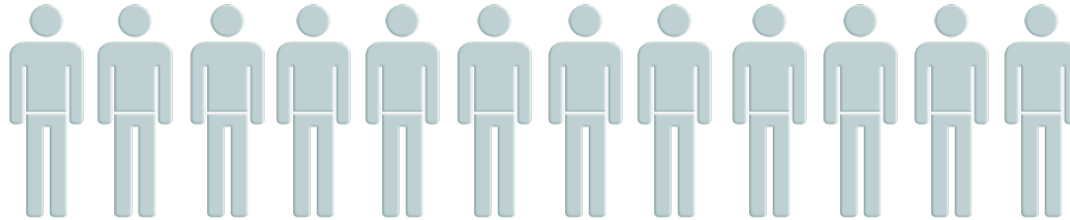
- OSTRiCH is a group of healthcare institutions that have come together with the purpose of improving the quality of rectal cancer care in the U.S. through advocacy, education, and research.
- At the institutional level, OSTRiCh members represent most facets of the U.S. healthcare delivery system; both large and small private clinics, university-affiliated hospitals, large healthcare systems, and smaller community hospitals



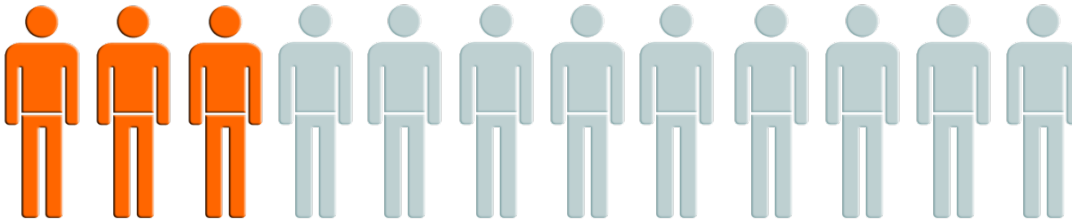
The OSTRiCh Consortium (Optimizing the Surgical Treatment of Rectal Cancer)

- The main components of rectal cancer treatment include
 1. Total mesorectal excision
 2. Assessment of the quality of surgery by pathologists
 3. Identification of patients at a high risk of local recurrence through imaging techniques
 4. Use of effective neoadjuvant and adjuvant therapies, including radiotherapy and chemotherapy
 5. MDT approach that identifies, coordinates, delivers, and monitors the ideal treatment on an individual basis

Many patients present with metastatic CRC



All patients with CRC



~25% of patients present with mCRC



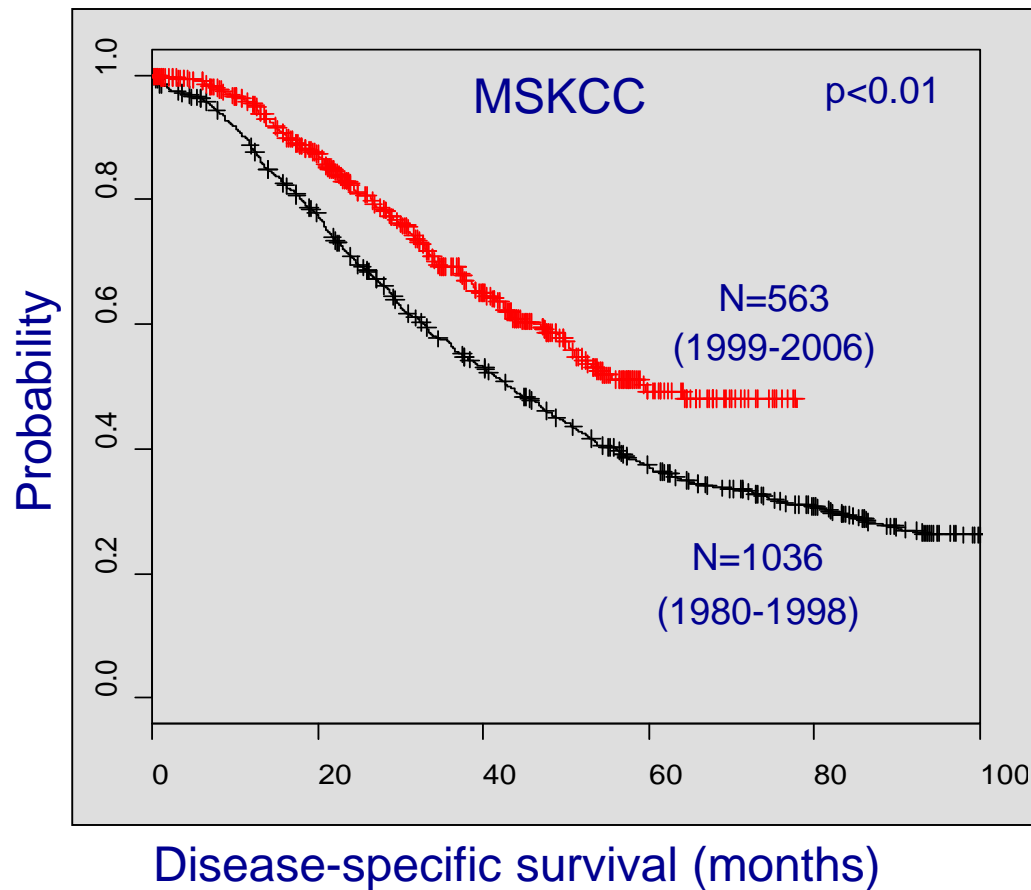
~50% of patients will develop metastases

The liver is the most common organ site for CRC metastases

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■ Resection for CRC Liver Metastases

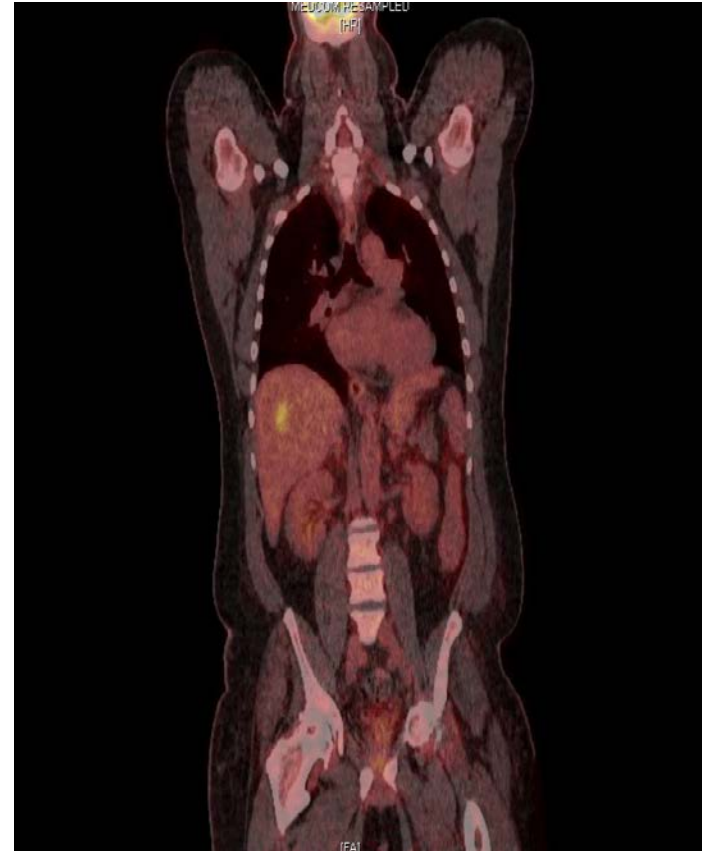


Improvements in survival over time

- Better chemotherapy
- Better imaging
- Better patient selection

Case discussion

- 60 year old female with sigmoid mass and solitary liver lesion, biopsy proven colon adenocarcinoma (synchronous)
- 52 year old male with Stage IIIC-T3, N2b, M0 colon cancer in the descending s/p 12 cycles of FOLFOX February 2017 and now with liver lesion concerning for metastasis (metachronous)



Synchronous metastases



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TREATMENT

Resectable^g synchronous liver
and/or lung metastases only

ADJUVANT TREATMENT^b

(resected metastatic disease)

Synchronous or staged colectomy^u with liver or lung
resection (preferred) and/or local therapy^v
or

Neoadjuvant therapy (for 2–3 months) FOLFOX
(preferred) or CAPEOX (preferred) or FOLFIRI
(category 2B) followed by synchronous or staged
colectomy^u and resection of metastatic disease
or

Colectomy^u followed by chemotherapy (for 2–3
months)
FOLFOX (preferred) or CAPEOX (preferred) or FOLFIRI
(category 2B) and staged resection of metastatic
disease

FOLFOX (preferred) or CAPEOX (preferred)
or
Capecitabine or 5-FU/leucovorin
(6 MO TOTAL PERIOPERATIVE TREATMENT
PREFERRED)

[See Surveillance \(COL-\)](#)

^bSee Principles of Imaging (COL-A).

^gSee Principles of Surgery (COL-C 2 of 3).

^uHepatic artery infusion ± systemic 5-FU/leucovorin (category 2B) is also an option at institutions with experience in both the surgical and medical oncologic aspects of this procedure.

^vResection is preferred over locally ablative procedures (eg, image-guided ablation or SBRT). However, these local techniques can be considered for liver or lung oligometastases (COL-C and COL-E).

Metachronous

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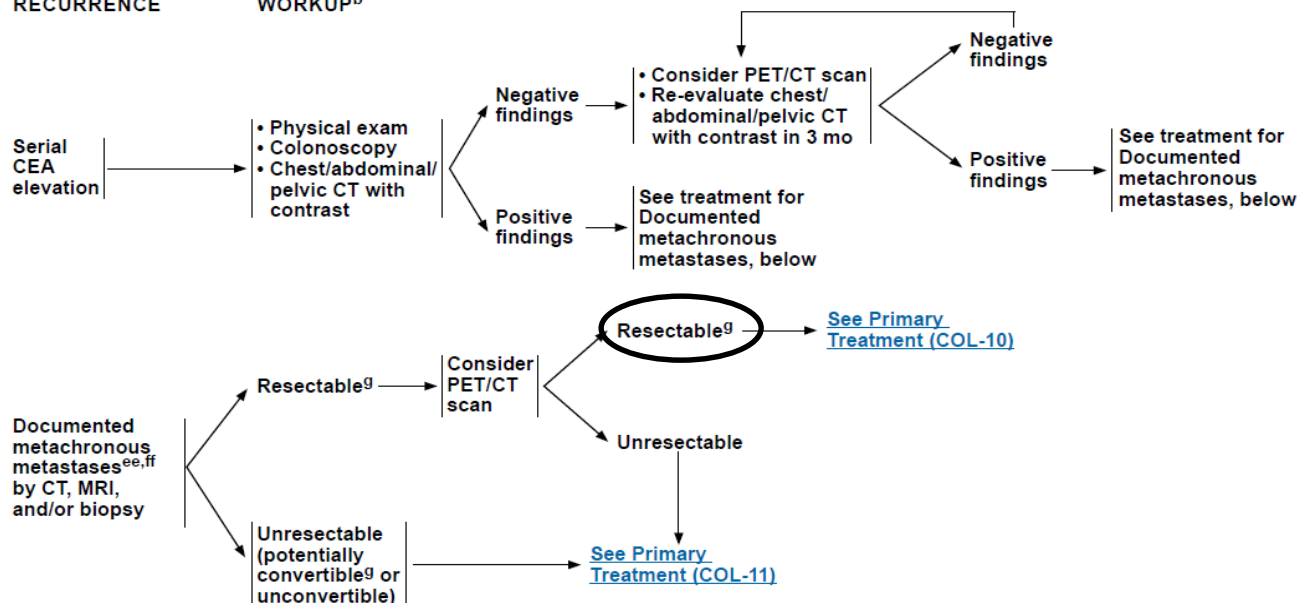
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RECURRENCE

WORKUP^b



^bSee Principles of Imaging (COL-A).

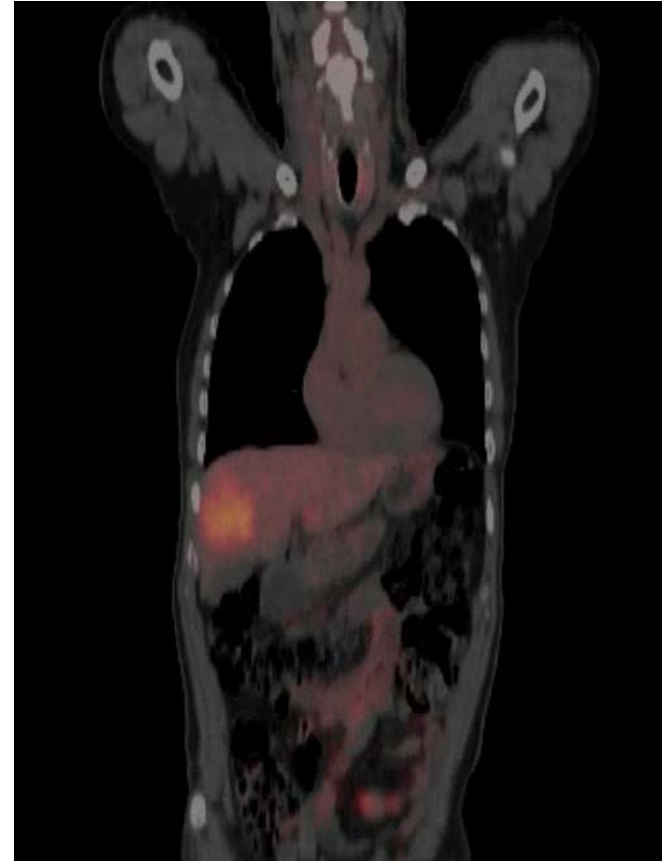
^gSee Principles of Surgery (COL-C 2 of 3).

^{ee}Determination of tumor gene status for *RAS* and *BRAF* (individually or as part of next-generation sequencing [NGS] panel). Determination of tumor MMR or MSI status (if not previously done). See Principles of Pathologic Review (COL-B 4 of 5) - *KRAS*, *NRAS* and *BRAF* Mutation Testing and Microsatellite Instability (MSI) or Mismatch Repair (MMR) Testing.

^{ff}Patients should be evaluated by a multidisciplinary team including surgical consultation for potentially resectable patients.

Case #2

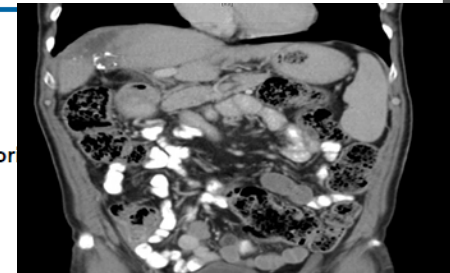
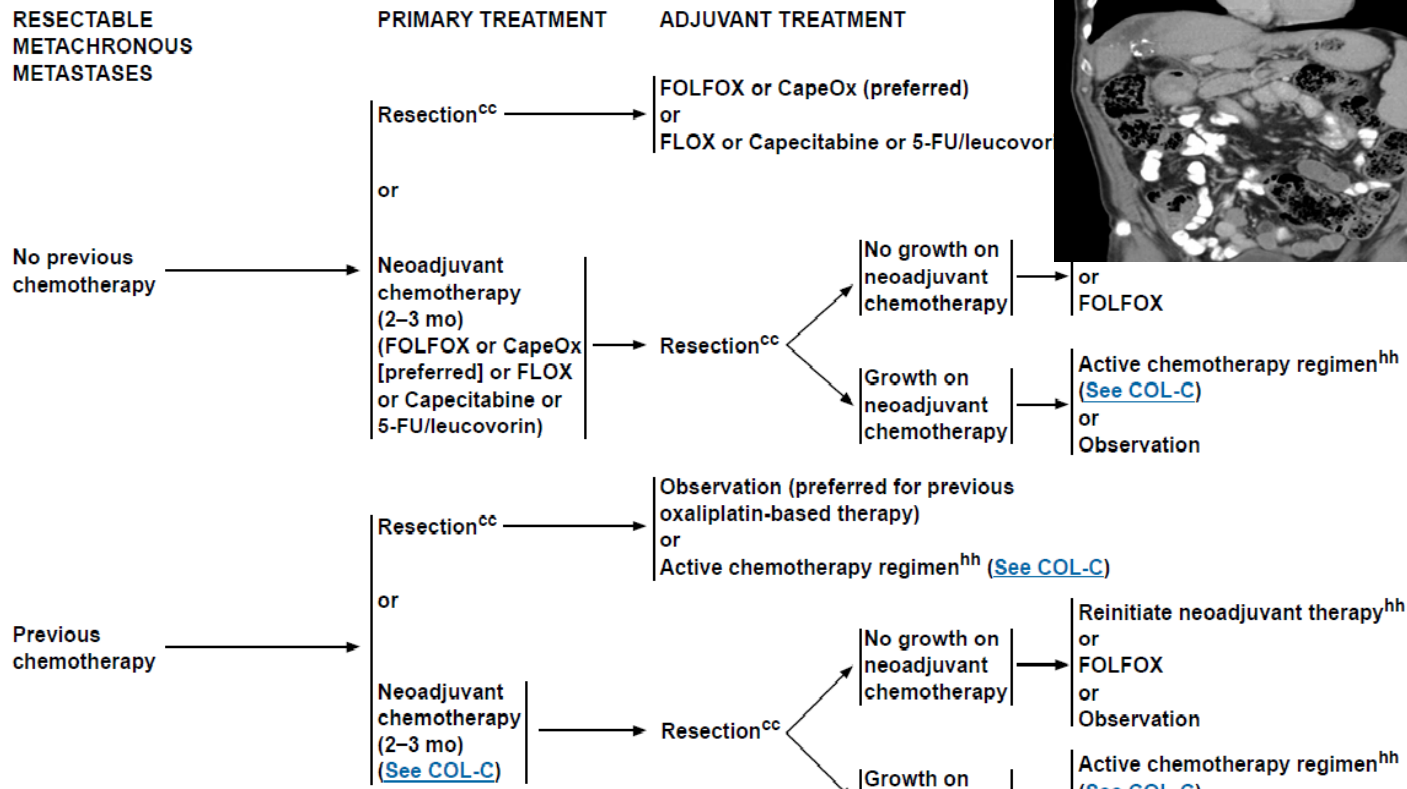
- 65 year old AAM presented with a left sided colon mass and a large liver mass. Biopsy proven colon cancer with metastasis to the liver
- Synchronous metastasis but not amenable to liver resection surgery upfront.



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RESECTABLE METACHRONOUS METASTASES



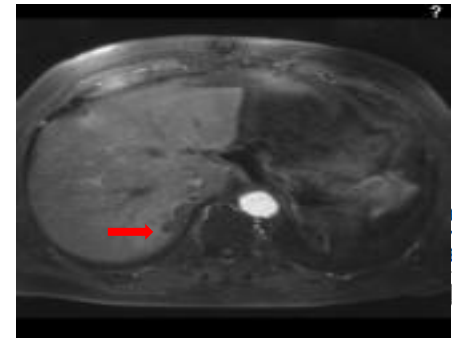
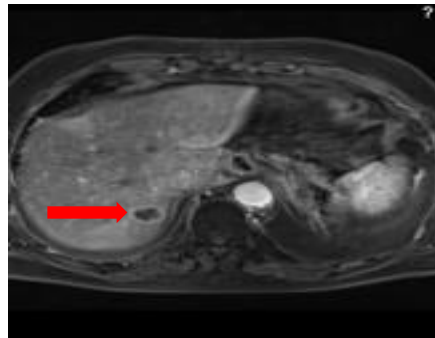
Resectable metastases

-Resection of a limited number of intrahepatic metastases

has been shown to provide long term benefit 5-yr Relapse Free Survival (RFS) after resection of isolated colorectal liver metastases is ~ 30% (20-46%); only 10% eligible.

-Non-surgical treatment options

Radiation Therapy-SBRT (Stereotactic body radiation therapy)
Delivery of a large dose of radiation therapy to extracranial lesions in typically 5 or fewer high dose treatments. Excellent 1-year local control (90%)

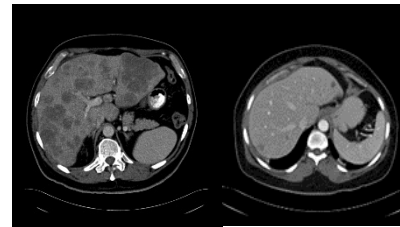


Local treatments options other than SBRT- Ablation

Ablation is a minimally invasive technique that destroys cancer cells directly. It is typically used to treat liver metastasis, but it can be used to treat other metastatic sites.

THERMAL

- Radiofrequency ablation
- Microwave ablation
- Cryoablation ablation

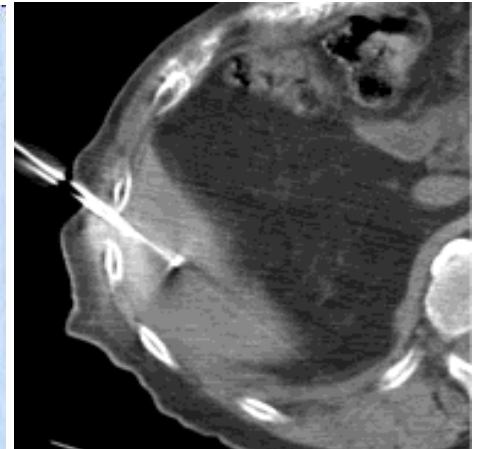
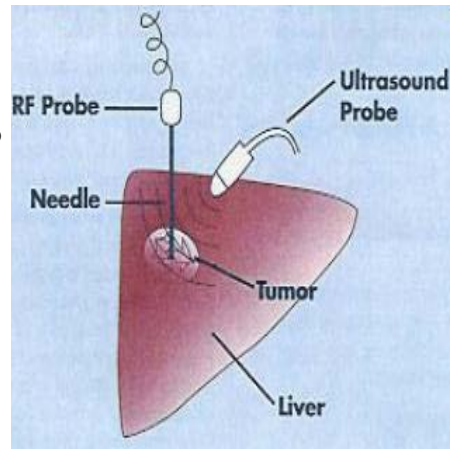


NON-THERMAL

- Chemical ablation: Ethanol and acetic acid
- IRE ablation – Irreversible electroporation

Radiofrequency ablation

- High-frequency alternating current flows from electrical probe through tissue to ground
- Indications
 - Less than 5 cms or 3 or fewer lesions < 3 cms
 - 3 year survival up to 55%; local r/c up to 30%
- Contraindication:
 - <1cm from vessels.
 - Proximity to bile ducts and gallbladder.
- Complication:
 - Pain – bleeding (intraperitoneal or sub-capsular), pleural effusions, pneumothorax, skin burn, cellulites.
 - Liver abscess (pts with bilo-enteric anastomoses).
 - Tumor seeding (pt with sub-capsular lesions, high grade HCC, high baseline AFP).
 - Post-ablation syndrome (32-58%) – hypoxemia, pain, fever and malaise for up to 3-4 weeks

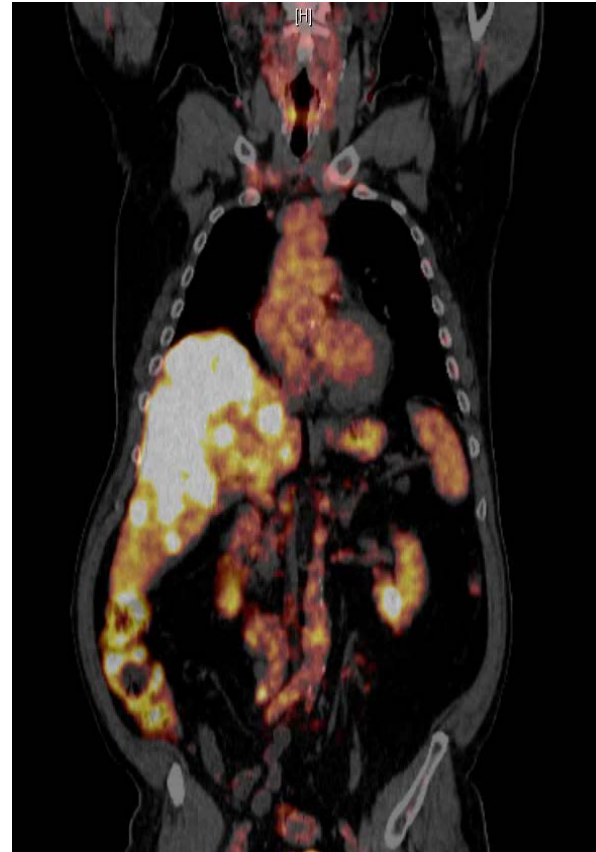


MICROWAVE ABLATION

- Indication: similar to RFA.
- Mechanism: electromagnetic field around the probe → agitation of water molecules around the probe to heat the tissue.
- Advantage:
 - Higher intra-lesion temperature/ Faster heating than RF.
 - Less affected by thermal conduction.
 - Less prone to heat sink effect.

Case #3

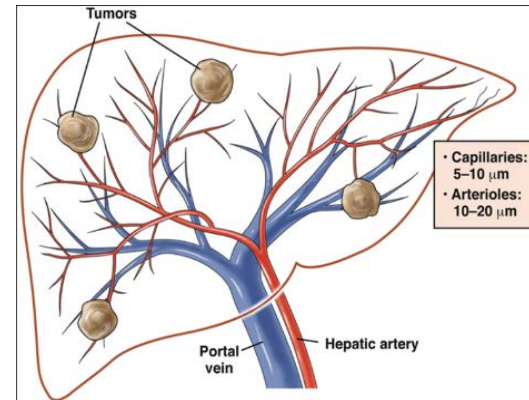
- Patient is 70 year old White male with synchronous metastasis from colon cancer.
- Unresectable, bilobar



Local therapies- Embolization

Embolization is a minimally invasive technique designed to block blood flow to the liver. Three primary types are:

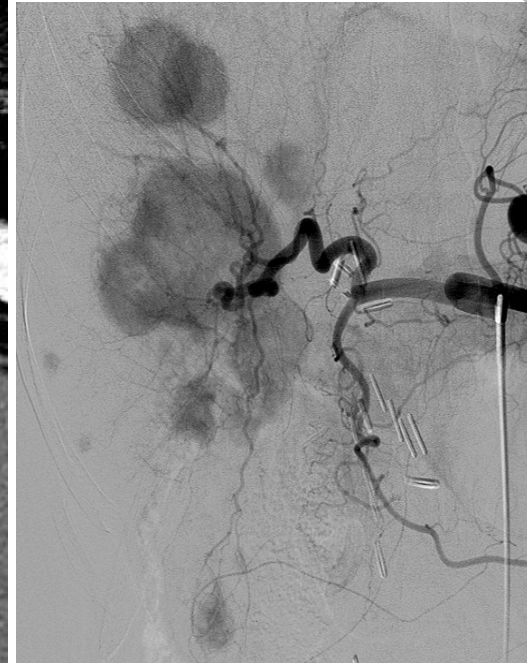
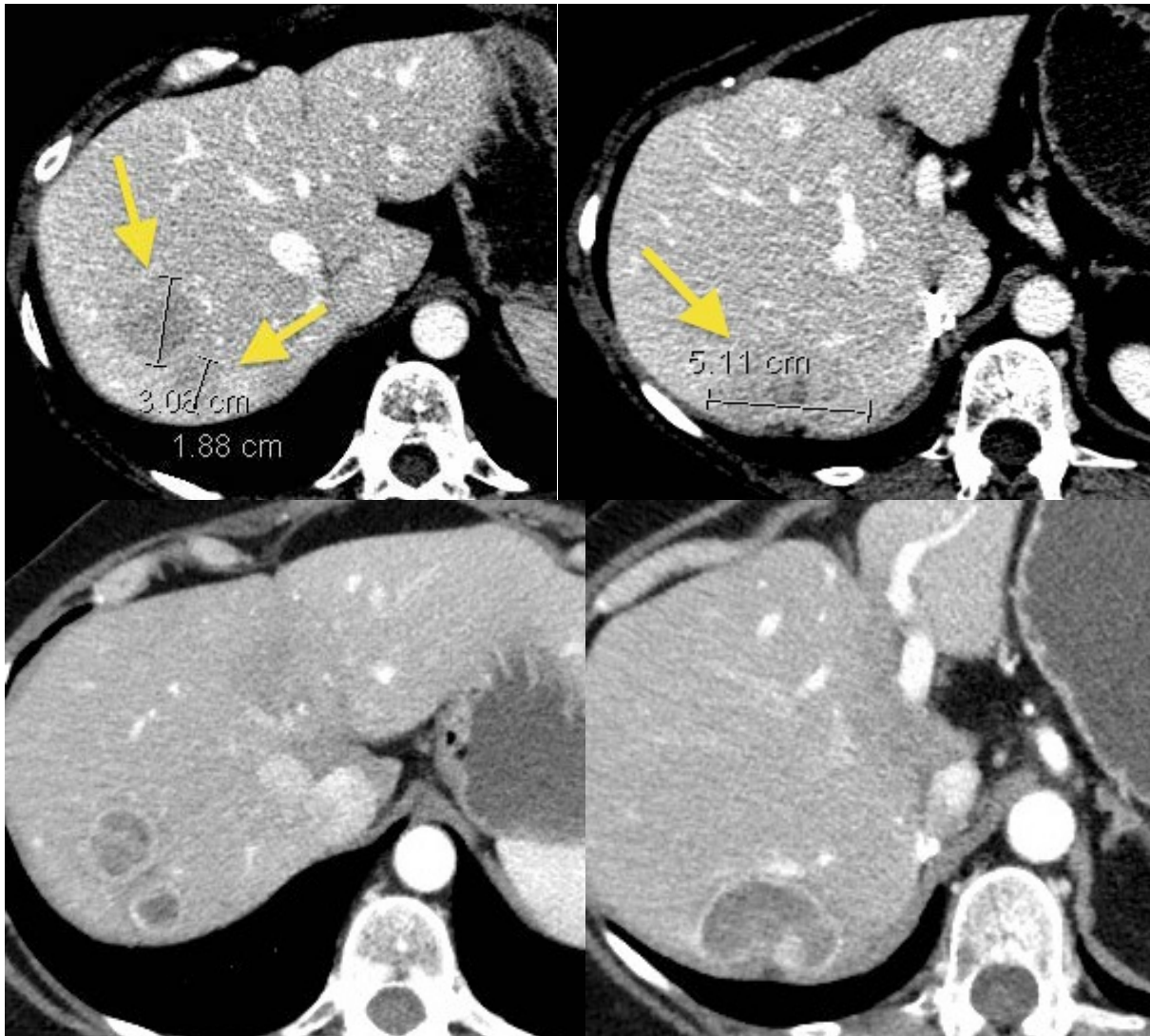
- Arterial embolization (trans-arterial embolization [TAE])
- Chemoembolization (trans-arterial chemoembolization [TACE])
- Radioembolization-radioactive isotopes



Radioembolization

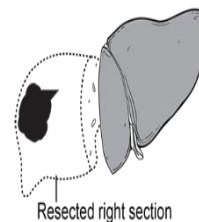
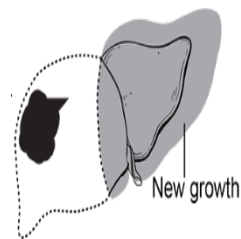
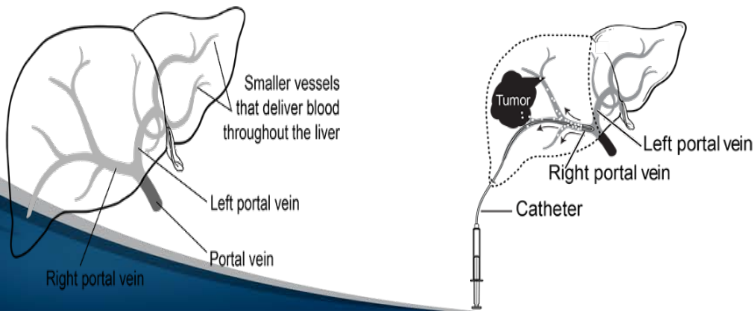
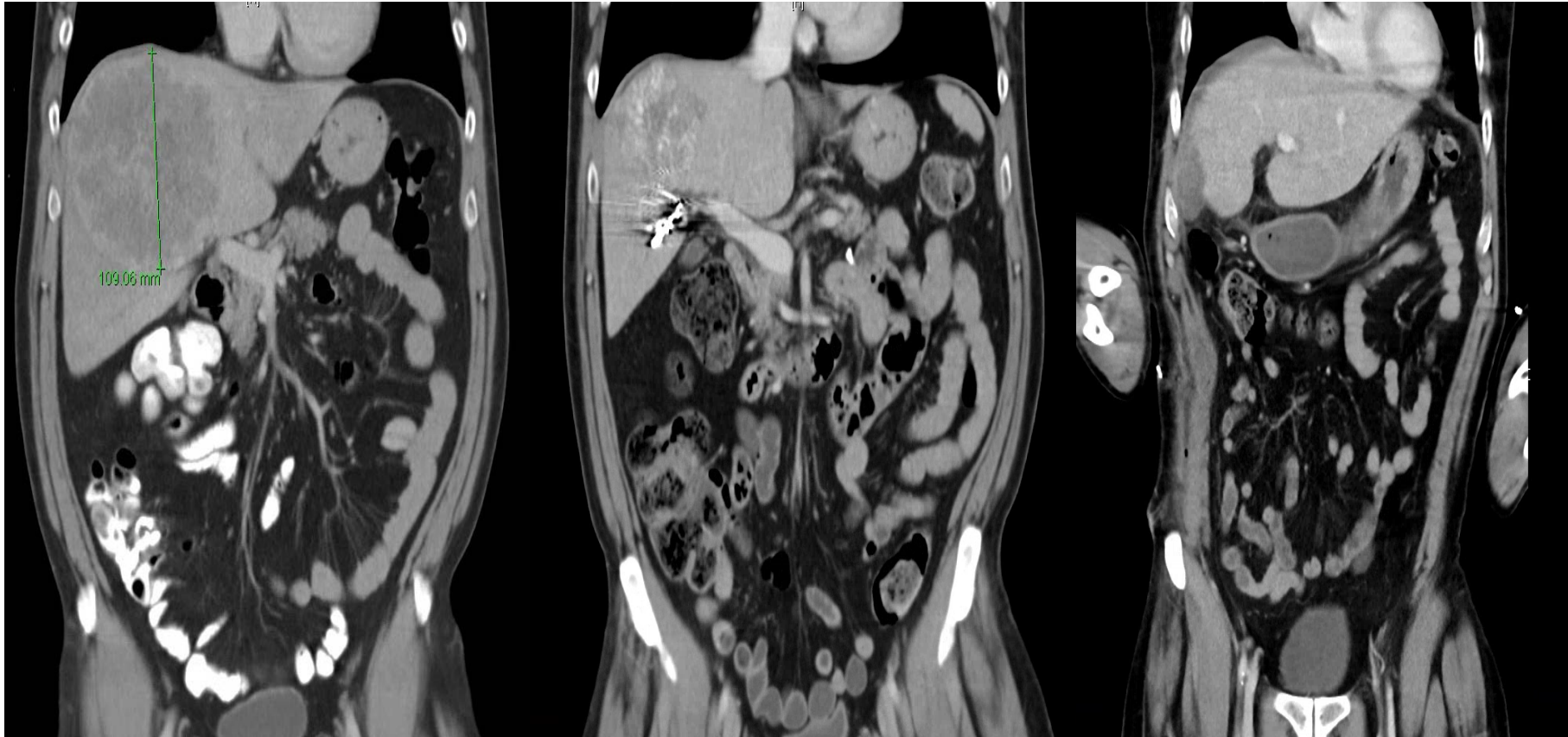
Radioactive isotopes (131 -labeled lipiodol or yttrium 90 [^{90}Y]-tagged glass or resin microspheres) that are delivered selectively to the tumor via the hepatic artery (selective internal radiotherapy [SIRT])

- Microspheres are delivered to the liver and intrahepatic tumor through a catheter placed into the hepatic artery, the primary blood supply to liver tumors.
- Since microspheres are unable to pass through the vasculature of the liver and liver tumor due to arteriolar capillary blockade, they are trapped and exert a local radiotherapeutic effect



Pre-treatment CT scans demonstrate multifocal metastases (Arrows). This finding is confirmed at angiography . Three months after radioembolization, there is extensive necrosis in the treated tumors .

■ Portal vein embolization



■ Peritoneal disease

- **Hyperthermic intraperitoneal chemotherapy (HIPEC)** is a highly concentrated, heated **chemotherapy** treatment that is delivered directly to the abdomen during surgery. Unlike systemic **chemotherapy** delivery, which **circulates** throughout the body, HIPEC delivers **chemotherapy** directly to cancer cells in the abdomen.

■ Future

The past:
One size fits all



MMR/MSI

RAS

BRAF



The future:
Individualized treatment



- Better identification of patient subgroups
- Dynamic monitoring of therapeutic effect and resistance

Questions?

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apparently reading about the causes of
cancer can give you cancer