Gebelik ve Laktasyon Döneminde Radyoterapi

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GÜTF Radyasyon Onkolojisi ABD

Olgu

- NG, 42 yaş
- Postpartum 3. ayda meme ca
- Bx: 0.5 cm invaziv duktal Ca, anterolateral CS (+)
  DCIS (+)
- MRM: rezidiv tümör yok, LN 0/18
- T1N0 meme ca, RT endikasyonu yok

Malignancies in Pregnancy 2

Breast cancer in pregnancy

Frédéric Amant, Sibylle Loibl, Patrick Neven, Kristel Van Calsteren

Lancet 2012; 379: 570–79

See Comment page 495

See Perspectives page 511

See *Lancet Oncol* Online/Articles

DOI:10.1016/S1470-2045(11)70363-1

This is the second in a Series of three papers about malignancies in pregnancy

Breast cancer staging and treatment are possible during pregnancy, and should be defined in a multidisciplinary setting. Tumour biology, tumour stage, and gestational stage at diagnosis determine the appropriate approach. Surgery for breast cancer is possible during all trimesters of pregnancy. Radiotherapy is possible during pregnancy but, dependent on the fetal dose received, can result in poor fetal outcomes. The decision to give radiotherapy should be made on an individual basis. Evidence increasingly supports administration of chemotherapy from 14 weeks' gestation onwards. New breast cancer treatments might be applicable to pregnant patients, but tamoxifen and trastuzumab are contraindicated during pregnancy. Cancer treatment during pregnancy will decrease the need for early delivery and thus prematurity, which is a major concern in management of breast cancer in pregnancy.

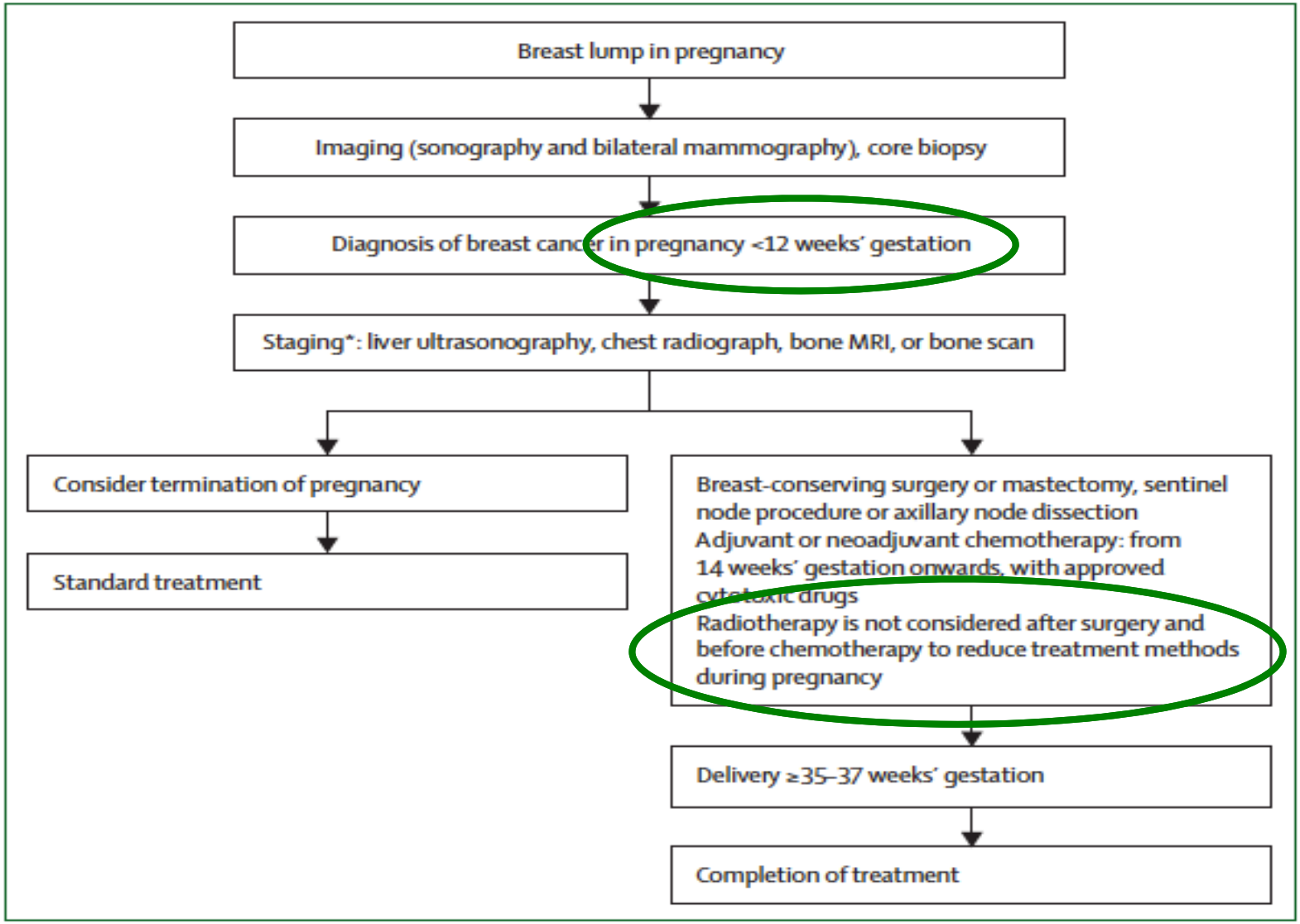

Figure 2: **Algorithm for treatment of breast cancer diagnosed during the first trimester of pregnancy**
*If results change clinical management, especially important during first trimester. Staging examinations and tumour biology assessment will affect the decision to continue pregnancy.

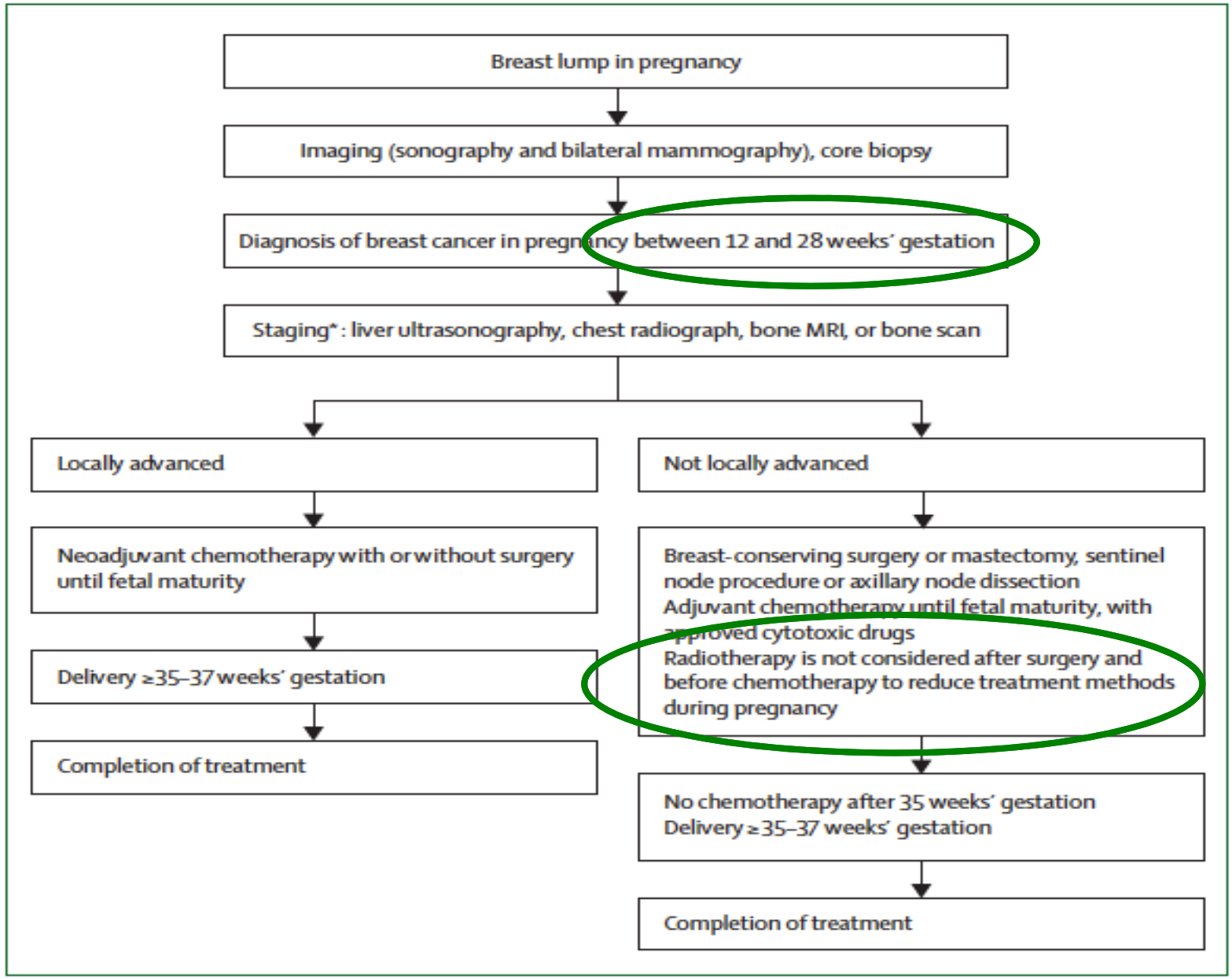

***Figure 3*: Algorithm for treatment of breast cancer diagnosed between 12 and 28 weeks of pregnancy**
*If results will change clinical management.

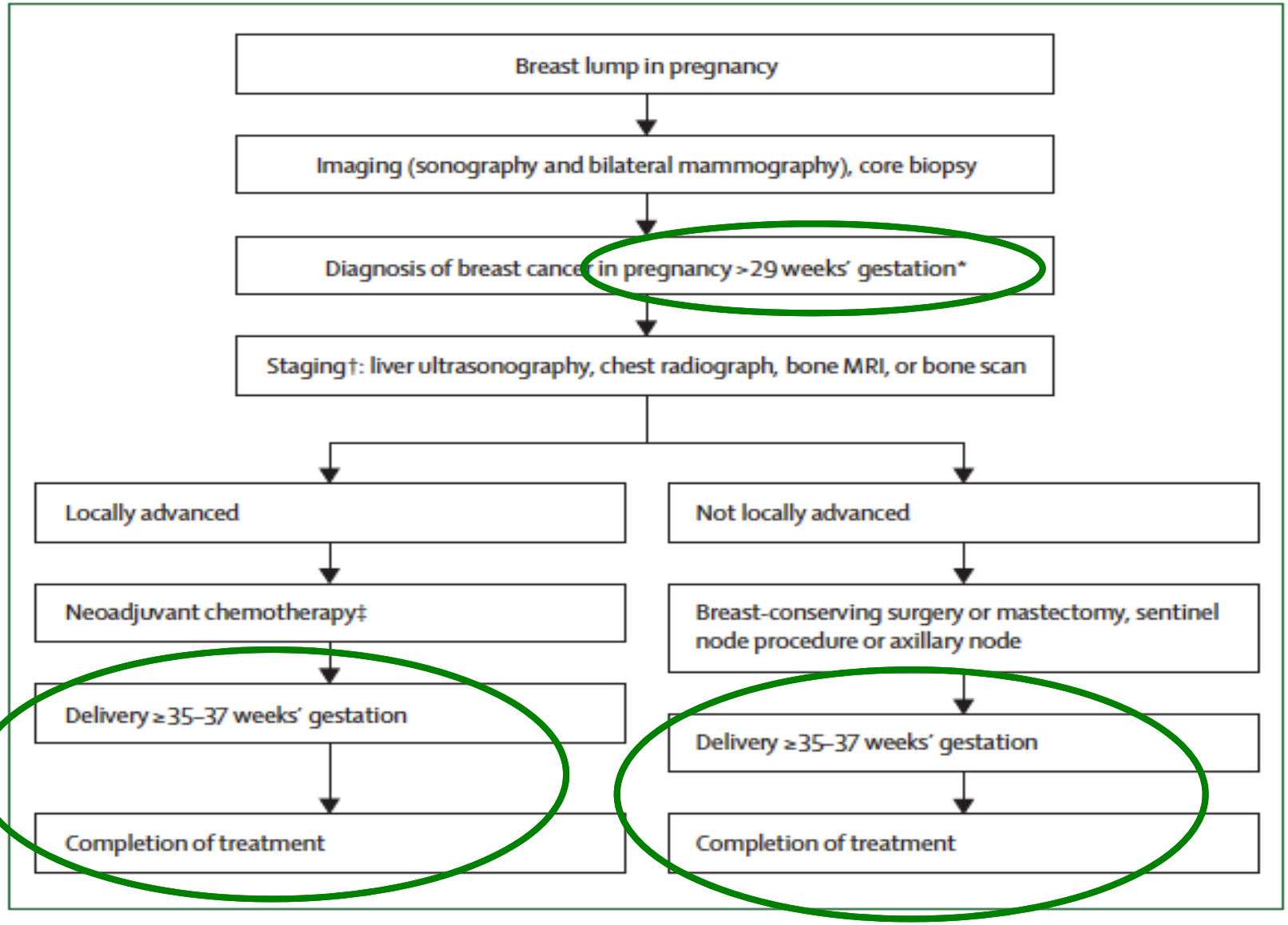

Figure 4: **Algorithm for treatment of breast cancer diagnosed from 29 weeks of pregnancy onwards**
*If diagnosed ≥35 weeks, consider delivery and post-partum staging and treatment. †If results will change clinical management. ‡If only one chemotherapy cycle is needed to reach fetal maturity, consider delivery at ≥35 weeks' gestation and all chemotherapy after delivery.

Panel: **Checklist for care of pregnant patients with breast cancer**

At diagnosis

- Confirm progressing pregnancy and define duration of pregnancy
- Exclude pre-existing fetal anomalies by ultrasonography before examinations or interventions

Obstetric follow-up during oncological treatment

- Consider intraoperative fetal monitoring from 24 to 26 weeks' gestation onwards, according to local policy
- Chemotherapy is possible during second or third trimester
  - Check for fetal wellbeing and general development
  - Check for preterm contractions
  - Check for intrauterine growth restriction
  - No chemotherapy after 35 weeks' gestation
- Radiotherapy is possible during first or second trimester
  - Check for fetal wellbeing and general development
  - Check for preterm contractions
  - Check for intrauterine growth restriction

Delivery

- Mode of delivery is determined by obstetric indications
- Timing of delivery
  - Preferably after 35–37 weeks' gestation
  - At least 3 weeks after last cycle of chemotherapy (delivered at 21 day intervals)
  - If preterm delivery is inevitable, fetal lung maturity is essential

Post-partum

- Examine placenta for metastatic disease
- Oncological treatment can be continued immediately after vaginal delivery, and a week after uncomplicated caesarean section
- Breastfeeding
  - If physiologically possible—eg, after radiotherapy
  - Contraindicated during and after chemotherapy

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Review

Breast cancer in pregnancy: Recommendations of an international consensus meeting ☆

Amant Frédéric [a,*,s], *Deckers Sarah* [b], *Van Calsteren Kristel* [b], *Loibl Sibylle* [c], *Halaska Michael* [d], *Brepoels Lieselot* [e], *Beijnen Jos* [f], *Cardoso Fatima* [g], *Gentilini Oreste* [h],

- RT, 1. ve 2. trimesterde uygulanabilir
- 3. trimesterde RT ertelenmelidir

clinical practice guidelines

Annals of Oncology 24 (Supplement 6): vi160–vi170, 2013
doi:10.1093/annonc/mdt199
Published online 27 June 2013

Cancer, pregnancy and fertility: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

F. A. Peccatori[1], H. A. Azim Jr[2], R. Orecchia[3], H. J. Hoekstra[4], N. Pavlidis[5], V. Kesic[6] & G. Pentheroudakis[5], on behalf of the ESMO Guidelines Working Group*

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- İlk trimesterde lokal tedavi dikkatli planlanmalıdır
- MKC yapıldığında RT'nin >6 ay gecikmesi, lokal rekürrens ihtimalini artırabilir

- RCT yok; veriler kohort çalışmalarına, vaka serilerine ve olgu sunumlarına dayanmakta

- ICRP raporu (1990): ‘’sağlam bir endikasyon olmadığı sürece hamile kadınlarda abdomenin radyasyona maruz kalacağı diagnostik ve terapötik prosedürlerden uzak kalınmalı’’

Radyasyonun etkileri-1

- ICRP raporları (2000, 2003)

-hayvan çalışmaları

-atom bombası, Hiroşima, (65 yıllık takip)

-Çernobil kazası (25 yıllık takip)

-diagnostik x-ışını

**Genel olarak intra-uterin radyasyon sonrası beklenen etkiler;

prenatal ölüm, malformasyon, MR ve kanser

Radyasyonun Etkileri-2

- 0-2 hafta: prenatal ölüm (eksperimantal data)

- 2-8 hafta: organogenezis,

  malformasyon gelişebilir ancak nadir

  Eşik dozu: 0.1-0.2 Gy

- 8-25 hafta: SSS IR'ya duyarlı

  0.1 Gy sonrası IQ azalır

  1 Gy ile ciddi MR gelişme riski var

  (MR riski %40; ileri yaşlarda IQ da 13-21 puan azalma)

  Eşik doz 8-15. haftadaki fetus için 0.06 Gy

  16-25. haftadaki fetus için 0.25 Gy

Radyasyonun Etkileri-3

0-38. hafta: Çocukluk çağı solid tümörleri ve lösemi gelişime riski

Çç da spontan ca ve lösemi gelişimi 2-3/1000

0.01 Gy fetus ışınlamasıyla bu risk 3-4/1000

Bazı çalışmalarda bu oran daha düşük 1/1700

Time after conception (weeks)	Effect	Risk per 0·01 Gy	Spontaneous frequency
0–2	Prenatal death*	0·01–0·001	0·3–0·6
3–8	Malformation*	0·005†	0·06
8–15	Mental retardation IQ decrease‡	0·004	0·005
16–25	Mental retardation IQ decrease§	0·001	0·005
0–38	Leukaemia, solid tumours in childhood	0·003–0·004	0·002–0·003

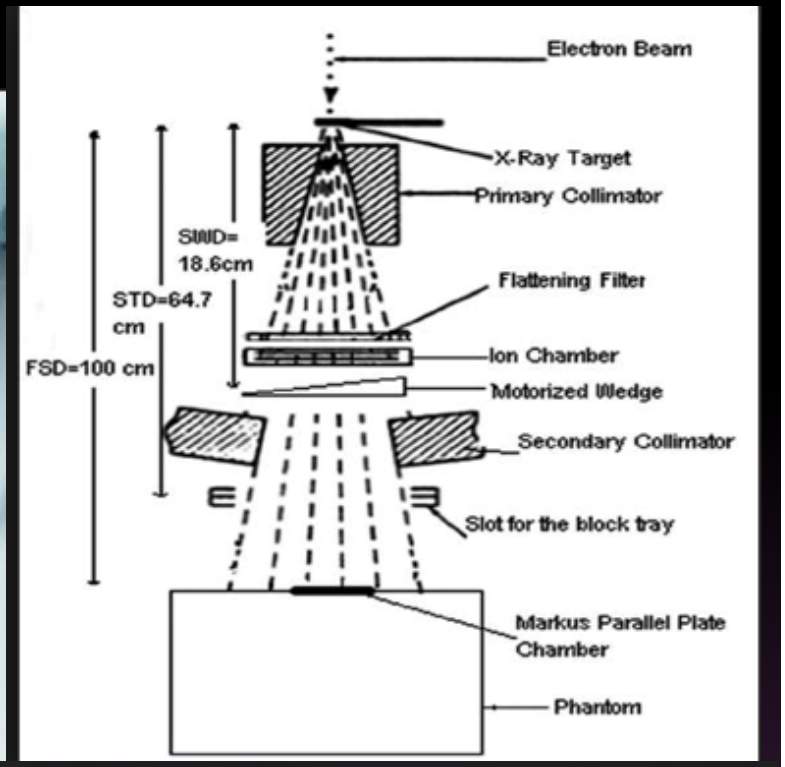
*Based on experimental data.[32] †Above threshold dose of 0·1–0·2 Gy.[33] ‡Reduction of 21 IQ points per 1 Gy above threshold of about 0·05 Gy;[33,34] threshold dose for mental retardation about 0·06 Gy;[35] §Reduction of 13 IQ points per 0·1 Gy above threshold dose of about 0·05 Gy;[33,34] threshold dose for mental retardation about 0·25 Gy.[35]

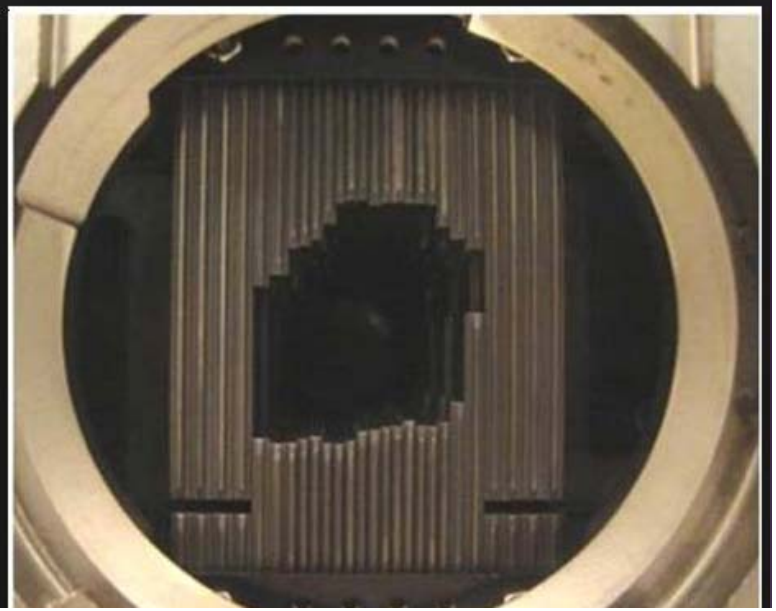
Table 1: **Effects and risks after exposure to ionising radiation in utero, and spontaneous frequency (without exposure)**

- RT tedavi alanı dışındaki absorbe doz (periferal doz: PD), fetus dozundan sorumlu

1. Tedavi cihazının kafasından gelen doz
2. Kolimatör, wedge ve bloklardan saçılan doz
3. Tedavi alanı içinden saçılan doz

**>10 MV üzerindeki dozlarda absorbe doza foton-nötron eklenmesi göz önünde bulundurulmalı


Electron Beam
X-Ray Target
Primary Collimator
SMD=
18.6cm
Flattening Filter
STD=64.7
cm
FSD=100 cm
Ion Chamber
Motorized Wedge
Secondary Collimator
Slot for the block tray
Markus Parallel Plate
Chamber
Phantom



- PD ve ilgili etkenler birçok çalışmada ve AAPM's T.G No:36 da değerlendirildi.
- PD aşağıdaki faktörlere bağımlı olarak değişir

1. RT alanından olan uzaklık (hamileliğin ileri döneminde önemli; fetus büyüdükçe RT alanına yaklaşır)
2. Dokunun derinliği
3. Alan boyutu

- Erken dönemde ışınlama

  6-25 MV x-ışını ile 8. haftada fetusun aldığı doz 0.03 Gy 24. haftada 0.2 Gy, 36. haftada 1.43 Gy*

- wedge kullanılmaması
- kurşun koruma (fetus dozu %50-75 azaltılabilir)

**Van der Giessen PH. Radiother Oncol 1997; 42:257-64*

ÖZET

- Genel öneri, hamilelikte RT'nin ertelenmesi
- 1. ve 2. trimesterda RT ile fetus dozlarının deterministik etkilerin ortaya çıkması için gerekli eşik dozun altında tutulabileceği ve sağlıklı çocuklar doğabileceği gösterilmiştir.
- Ancak bu çalışmalarda kullanılan enerji, RT alanı ve blok, MLC, wedge, koruma bloğu kullanımı farklılık göstermekte; birebir karşılaştırma yapmak zor.
- Her hasta için ayrı ölçüm yapılarak olası riskler hesaplanmalı ve bu riskler hasta ve ailesi ile paylaşılarak tedavi kararı alınmalı.

Laktasyon Döneminde RT

***Panel:* Checklist for care of pregnant patients with breast cancer**

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  - If physiologically possible—eg, after radiotherapy
  - Contraindicated during and after chemotherapy

- MKC ve RT sonrası bazı klinisyenler süt verilmesini önermemekte; ancak bu görüşü destekleyen yayın yok
- Son yayınlar emzirmenin uygun ve güvenilir olduğunu bildirmekte
- Meme RT'sinden sonra laktasyonla ilgili az sayıda veri mevcut
- Emzirilen bebeklerdeki etkiler???

- Işınlanan memede hipoplazi, hipotrofi
- Meme başında retraksiyon
- Emzirirken meme başında ağrı rahatsızlık hissi
- Hastaların %50'sinde laktasyon devam etmekte ancak sütün hacimi azalmakta (%70-80)
- Karşı memede laktasyon etkilenmemekte

**Leal SC, Expert Rev Anticancer Ther, 2013; 13 (2): 159-64.*

Characteristics	Actual case		Previous case	
	Treated breast	Untreated breast	Treated breast	Untreated breast
Density	1.037	1.044	1.035	1.042
Na (mmol/l)	28.7	8.5	29.3	8.2
K (mmol/l)	12.2	14.4	12.8	14.3
Phosphates (mg/dl)	2.4	6.2	2.6	6.3
Triglycerides (mg/dl)	1531.0	3578.0	1548.0	3619.0
LDH (U/dl)	269.0	344.0	274.0	353.0
GOT (U/dl)	35.0	44.0	34.0	51.0
GPT (U/dl)	54.0	66.0	49.0	85.0
Alkaline phosphate (IU/dl)	92.0	83.0	89.0	52.0
Albumin (g/dl)	1.8	1.6	1.3	1.56