Hypofractionnement et reconstruction par prothèse mammaire

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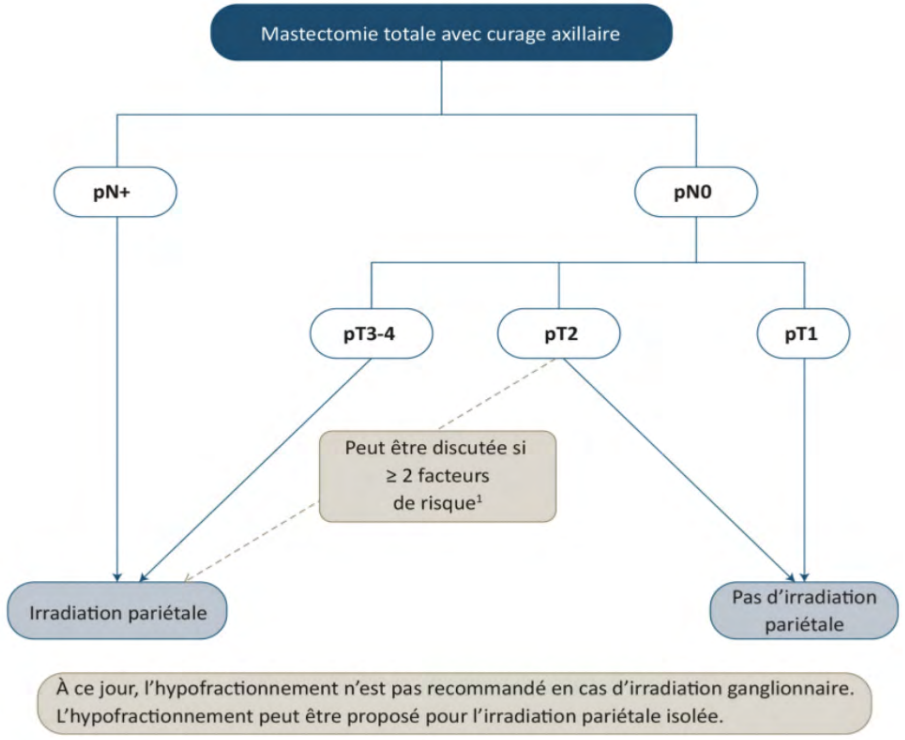
Conflits d’intérêt

Introduction : prothèse mammaire & PMRT

- 20 000 mastectomies par an en France
- Environ 20% de reconstruction mammaire immédiate (RMI)
- Prothèse : expandeur ou prothèse immédiate

- Indications de radiothérapie post-mastectomie (PMRT) +/- irradiation des aires ganglionnaires



Introduction : RT hypofractionnée

The UK Standardisation of Breast Radiotherapy (START) Trial B of radiotherapy hypofractionation for treatment of early breast cancer: a randomised trial

The START Trialists' Group*

Long-Term Results of Hypofractionated Radiation Therapy for Breast Cancer

Timothy J. Whelan, B.M., B.Ch., Jean-Philippe Pignol, M.D., Mark N. Levine, M.D., Jim A. Julian, Ph.D., Robert MacKenzie, M.D., Sameer Parpia, M.Sc., Wendy Shelley, M.D., Laval Grimard, M.D., Julie Bowen, M.D., Himu Lukka, M.D., Francisco Perera, M.D., Anthony Fyles, M.D., Ken Schneider, M.D., Sunil Gulavita, M.D., and Carolyn Freeman, M.D.

- Efficacité et tolérance comparables aux schémas normofractionnés
- Amélioration de la qualité de vie

  - START B : peu de mastectomies (<10%) ; pas de RMI
  - Whelan : pas de mastectomie

⇒ ***Pas de données concernant l'hypofractionnement en cas de PMRT avec RMI par prothèse***

⇒ ***Quelle qualité de vie ? Quelle toxicité attendre de la RT hypofractionnée ?***

(Contracture ? Coque ? Infections ? Rupture ? …)

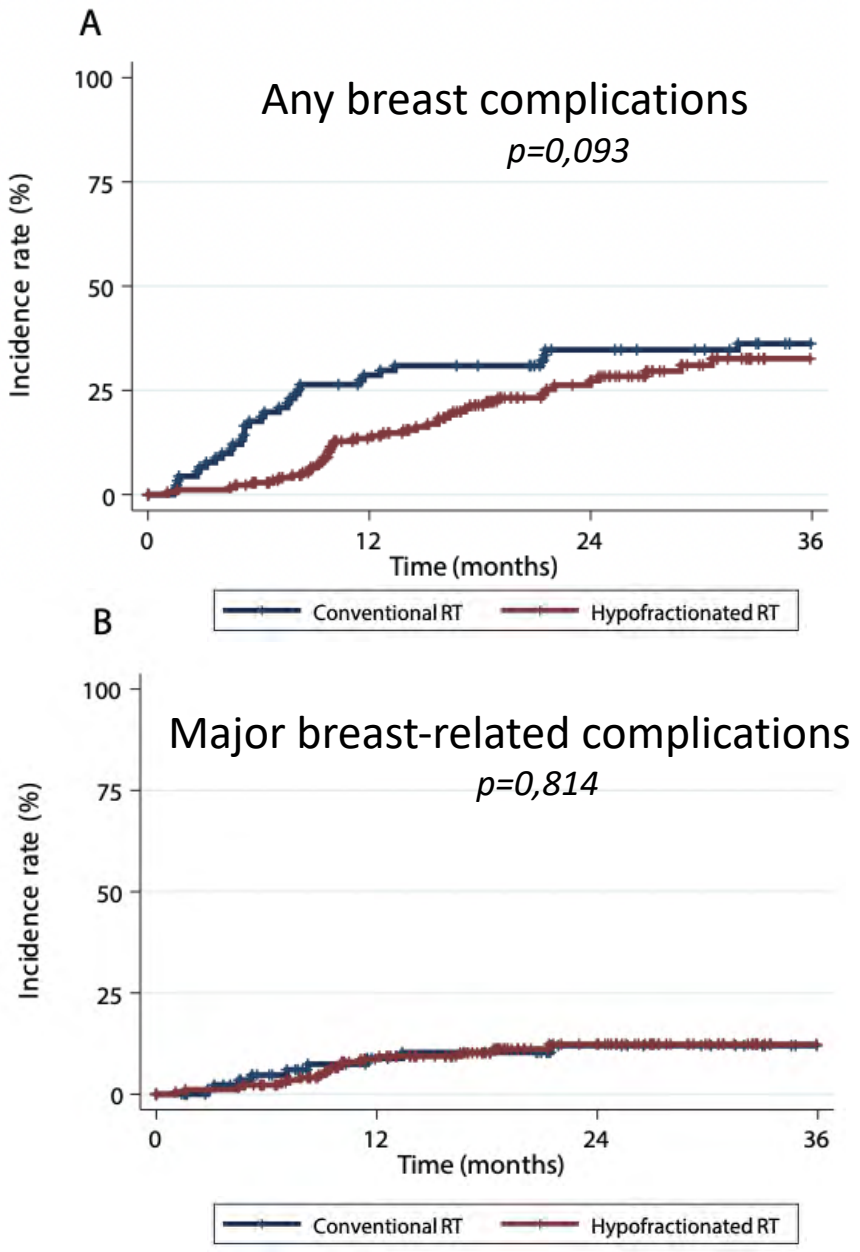
Avant 2024

Influence of Hypofractionated Versus Conventional Fractionated Postmastectomy Radiation Therapy in Breast Cancer Patients With Reconstruction

Dong-Yun Kim, MD,* Eonju Park, MD,† Chan Yeong Heo, MD, PhD,† Ung Sik Jin, MD, PhD,† Eun Kyu Kim, MD, PhD,‡ Wonshik Han, MD, PhD,‡,§ Kyung Hwan Shin, MD, PhD,* and In Ah Kim, MD, PhD*,§,‖

Etude rétrospective
Publiée en 2019
Unicentrique (Chine)
396 patientes (267 RMI)
Traitées entre 2009 et 2018

=> Nécessité de données prospectives



En 2024

- **Etude FABREC :** randomized trial of fractionation after breast reconstruction (Août 2024)

- **Méta-analyse :** postoperative complications of hypofractionated and conventional fractionated radiation therapy in patients with implant-based breast reconstruction (Octobre 2024)

- **Etude RT CHARM :** randomized trial of hypofractionated PMRT in woman with breast reconstruction (ASTRO 2024)

En 2024

- **<u>Etude FABREC :</u>** randomized trial of fractionation after breast reconstruction

Evaluer l'évolution du bien-être physique après une irradiation hypofractionnée versus normofractionnée dans le cadre d'une radiothérapie post-mastectomie avec reconstruction mammaire immédiate par prothèse

JAMA Oncology | Original Investigation

Hypofractionated vs Conventionally Fractionated Postmastectomy Radiation After Implant-Based Reconstruction

A Randomized Clinical Trial

Julia S. Wong, MD; Hajime Uno, PhD; Angela C. Tramontano, MPH; Lauren Fisher, MPH; Catherine V. Pellegrini, BS; Gregory A. Abel, MD, MPH; Harold J. Burstein, MD, PhD; Yoon S. Chun, MD; Tari A. King, MD; Deborah Schrag, MD, MPH; Eric Winer, MD; Jennifer R. Bellon, MD; Matthew D. Cheney, MD, PhD; Patricia Hardenbergh, MD; Alice Ho, MD, MBA; Kathleen C. Horst, MD; Janice N. Kim, MD; Kara-Lynne Leonard, MD, MS; Meena S. Moran, MD; Catherine C. Park, MD; Abram Recht, MD; Daniel E. Soto, MD, MS; Ron Y. Shiloh, MD; Susan F. Stinson, MD; Kurt M. Snyder, MD; Alphonse G. Taghian, MD, PhD; Laura E. Warren, MD; Jean L. Wright, MD; Rinaa S. Punglia, MD, MPH

Design

POPULATION

400 Women

Patients with breast cancer undergoing implant-based reconstruction and postmastectomy radiation

Median (range) age, 47 (23-79) y

SETTINGS / LOCATIONS

16 Hospitals in the US

INTERVENTION

400 Patients randomized

201 Conventional fractionation (CF)
Postmastectomy radiation therapy to a dose of 5000 cGy given over 25 treatments

199 Hypofractionation (HF)
Postmastectomy radiation therapy to a dose of 4256 cGy given over 16 treatments

PRIMARY OUTCOME

Change in physical well-being (PWB) derived from the PWB domain of Functional Assessment of Cancer Therapy–Breast quality-of-life instrument at 6 mo. PWB scores range from 0 to 28, with higher scores indicating better physical well-being.

Exclusion :
- T4
- ATCD de RT homolatérale
- RT bilatérale
- Maladie intercurrente non contrôlée

Pas de chimiothérapie concomitante

Stratification :
- Age (<45 ans ; > 45 ans)
- Centre de traitement

Matériels & méthodes

PHYSICAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
I have a lack of energy.....	0	1	2	3	4
I have nausea.....	0	1	2	3	4
Because of my physical condition, I have trouble meeting the needs of my family.....	0	1	2	3	4
I have pain.....	0	1	2	3	4
I am bothered by side effects of treatment.....	0	1	2	3	4
I feel ill.....	0	1	2	3	4
I am forced to spend time in bed.....	0	1	2	3	4

Population

Characteristic	No. (%)	
	Conventional therapy (n = 201)	Hypofractionated therapy (n = 199)
Patient characteristics		
Age, y		
<40	41 (21.4)	42 (21.7)
40-50	90 (46.9)	84 (43.3)
51-60	42 (21.9)	49 (25.3)
≥60	19 (9.9)	19 (9.8)
Missing, No.	9	5
BMI		
<20	11 (5.5)	18 (9.1)
20.0-24.9	75 (37.5)	79 (39.9)
25.0-29.9	60 (30.0)	55 (27.8)
30.0-34.9	34 (17.0)	30 (15.2)
≥35.0	20 (10.0)	16 (8.1)
Missing, No.	1	1
Smoking status		
Never smoked	140 (69.7)	147 (73.9)
Current or former smoker	61 (30.4)	52 (26.1)
Prior infection		
No	187 (93.0)	188 (94.5)
Yes	14 (7.0)	11 (5.5)
Cancer characteristics		
Laterality		
Right	93 (46.5)	113 (56.8)
Left	107 (53.5)	86 (43.2)
Missing	1	0

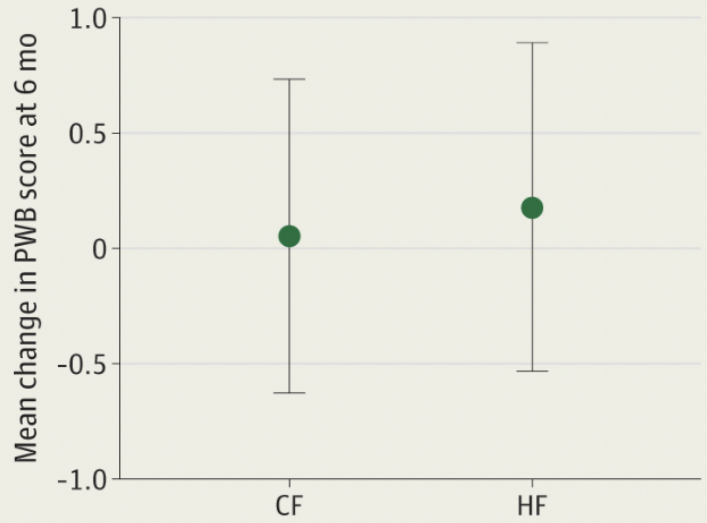
Characteristic	No. (%)	
	Conventional therapy (n = 201)	Hypofractionated therapy (n = 199)
Total No. of positive nodes		
0	52 (26.8)	56 (29.2)
1	76 (39.2)	65 (33.9)
2	32 (16.5)	33 (17.2)
≥3	34 (17.5)	38 (19.8)
Missing	7	7
Treatment characteristics		
Surgery		
Axillary node dissection		
No	112 (55.7)	99 (49.8)
Yes	89 (44.3)	100 (50.3)
No. of axillary nodes removed, median (range)	9.0 (0-27)	8.5 (0-36)
Location of device		
Prepectoral	118 (59.9)	115 (57.7)
Subpectoral	79 (40.1)	84 (42.2)
NA or unknown	4	0
Device irradiated		
Expander	156 (77.6)	160 (80.4)
Implant	45 (22.4)	39 (19.6)
Systemic therapy		
Neoadjuvant chemotherapy		
Yes	134 (66.7)	137 (68.8)
No	67 (33.3)	62 (31.2)
Unknown	0	0

Characteristic	No. (%)	
	Conventional therapy (n = 201)	Hypofractionated therapy (n = 199)
Neoadjuvant endocrine therapy		
Yes	39 (19.4)	46 (23.2)
No	162 (80.6)	152 (76.8)
Unknown	0	1
Radiation therapy		
Chest wall and nodes	160 (87.4)	170 (90.0)
Chest wall alone	23 (12.6)	19 (10.1)
Missing due to study withdrawal	9	5
Technique		
IMRT	78 (41.0)	82 (42.9)
Three-dimensional conformal	112 (59.0)	109 (57.1)
Missing	2	3
Time from surgery to radiation therapy, median (IQR), mo	2.7 (1.8-5.3)	2.4 (1.8-4.9)

Résultats

FINDINGS

There was no significant difference in the change in PWB scores at 6 mo between the 2 treatment groups (difference: 0.13; 95% CI, -0.86 to 1.11; *P*=.80)



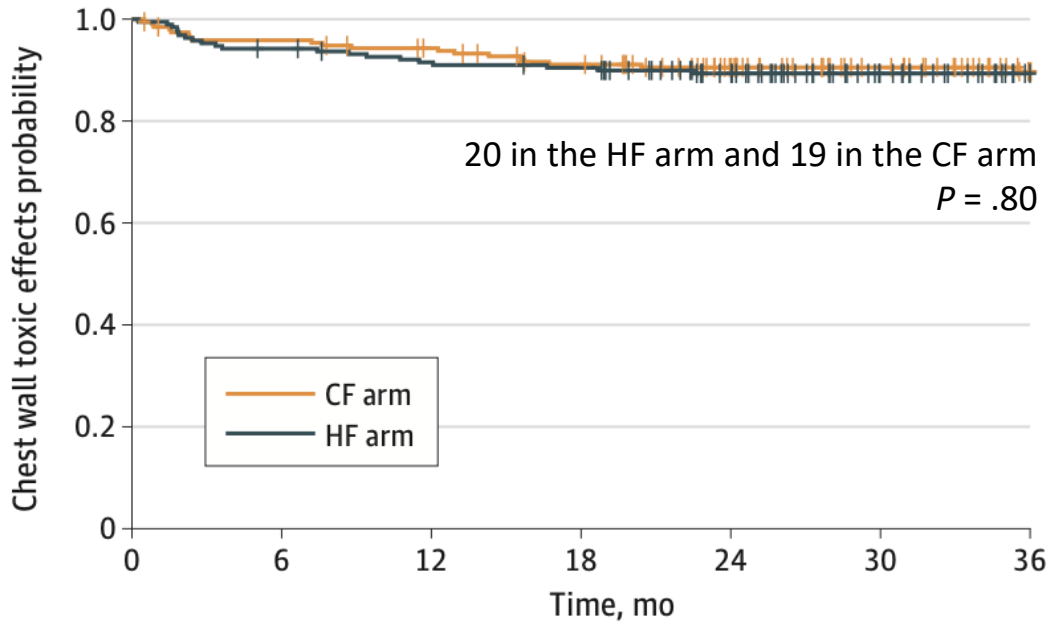
Mean change in PWB scores at 6 mo:
CF: 0.05 (95% CI, -0.63 to 0.74)
HF: 0.18 (95% CI, -0.53 to 0.88)

Table 2. Models for the Primary Outcome Adjusted for Patient Age

Variable	Estimate (SE) [95% CI]	*P* value
Model controlling for age		
CF therapy	1.0 [Reference]	NA
HF therapy	0.13 (0.50) [−0.86 to 1.11]	.80
Age group, y		
<45	1.0 [Reference]	NA
≥45	−0.21 (0.51) [−1.21 to 0.80]	.68
Subgroup analysis of age		
Age <45 y		
CF therapy	1.0 [Reference]	NA
HF therapy	1.46 (0.83) [−0.18 to 3.11]	.08
Age >45 y		
CF therapy	1.0 [Reference]	NA
HF therapy	−0.73 (0.62) [−1.95 to 0.49]	.24
Model with age interaction		
CF therapy	1.0 [Reference]	NA
HF therapy	1.46 (0.80) [−0.10 to 3.03]	.07
Age group, y		
<45	1.0 [Reference]	NA
≥45	0.87 (0.71) [−0.54 to 2.27]	.23
Study arm and age interaction		.03[a]
<45 y and CF therapy	−0.32 (0.45) [−1.20 to 0.56]	.47
<45 y and HF therapy	0.40 (0.45) [−0.49 to 1.30]	.38
≥45 y and CF therapy	1.00 (0.57) [−0.13 to 2.13]	.08
≥45 y and HF therapy	−0.46 (0.55) [−1.55 to 0.62]	.40

Résultats

Figure 2. Kaplan-Meier Plot for Freedom From Chest Wall Toxic Effects by Treatment Arm



*Chest wall toxic effects were defined **as any grade 3 or higher adverse** event after PMRT began (infection, delayed wound healing, TE or implant removal, or unplanned surgical intervention)*

Median follow up : 40,4 months

Table 3. Multivariable Cox Proportional Hazards Regression Model for Chest Wall Toxic Effects

Variable	HR (95% CI)	*P* value
Treatment arm		
CF treatment	1.0 [Reference]	NA
HF treatment	1.02 (0.52-2.00)	.95
Age, y		
<40	1.0 [Reference]	NA
40-50	1.65 (0.65-4.17)	.29
51-60	1.32 (0.46-3.78)	.60
≥60	0.89 (0.18-4.45)	.88
Time from surgery to PMRT, mo	0.99 (0.84-1.17)	.92
Postoperative infection		
No	1.0 [Reference]	NA
Yes	3.19 (1.18-8.65)	.02
Device irradiated		
Permanent implant	1.0 [Reference]	NA
Expander	4.44 (1.05-18.75)	.04
Neoadjuvant endocrine therapy		
No	1.0 [Reference]	NA
Yes	2.8 (1.42-5.5)	.003
No. of nodes removed (continuous)	1.06 (1.02-1.1)	.008

Discussion

- Pas de différence dans l'évolution du bien-être physique à 6 mois entre un schéma d'irradiation hypofractionné vs normofractionné
- Meilleure évolution du bien-être physique pour les patientes < 45 ans avec un schéma hypofractionné
- Faible taux de toxicité grave
- Limites : critère de jugement principal : score de qualité de vie , pas de données sur le contrôle loco-régional

En 2024

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- **Méta-analyse :** postoperative complications of hypofractionated and conventional fractionated radiation therapy in patients with implant-based breast reconstruction (Octobre 2024)

Postoperative complications of hypofractionated and conventional fractionated radiation therapy in patients with implant-based breast reconstruction: A systematic review and meta-analysis

Seong-Hyuk Park [a,1], Yun-Jung Yang [b,1], Sihyun Sung [c], Yelim Choi [c], Eun-Jung Yang [a,*]

[a] *Department of Plastic & Reconstructive Surgery, Institute of Innovative Digital Healthcare, Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea*
[b] *Department of Convergence Science, College of Medicine, Catholic Kwandong University International St. Mary's Hospital, Incheon, Republic of Korea*
[c] *Department of Research and Development, Seoul Medical Informatics Intelligence Lab Inc, Seoul, Republic of Korea*

En 2024

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[b] Department of Convergence Science, College of Medicine, Catholic Kwandong University International St. Mary's Hospital, Incheon, Republic of Korea
[c] Department of Research and Development, Seoul Medical Informatics Intelligence Lab Inc, Seoul, Republic of Korea

Méta analyse
Publiée en 2024
7 études
924 reconstructions par implants
51,2 Gy vs 43, 8 Gy
Suivi entre 10 et 35 mois

Schéma hypofractionné associé à des taux plus faibles de :
- contractures
- réintervention
- déhiscence de la cicatrice

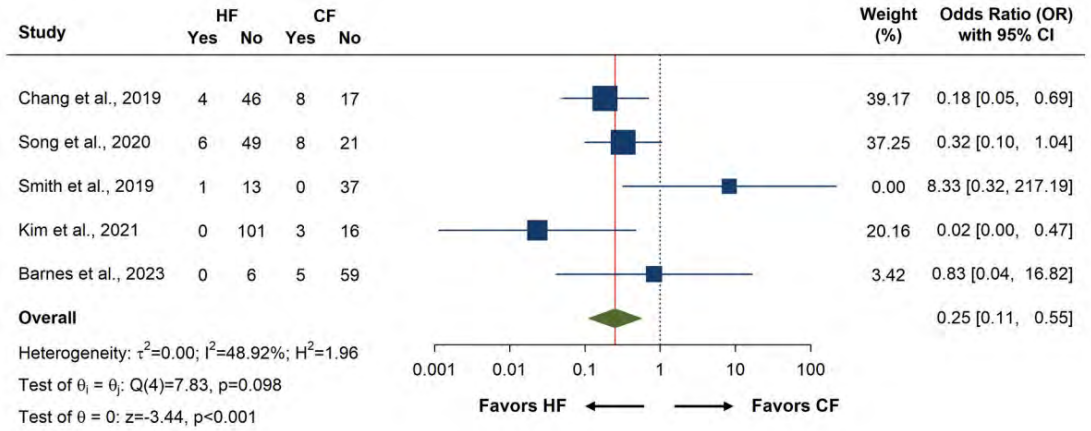

Fig. 2. Forest plot comparing incidence of capsular contracture between HF and CF groups.

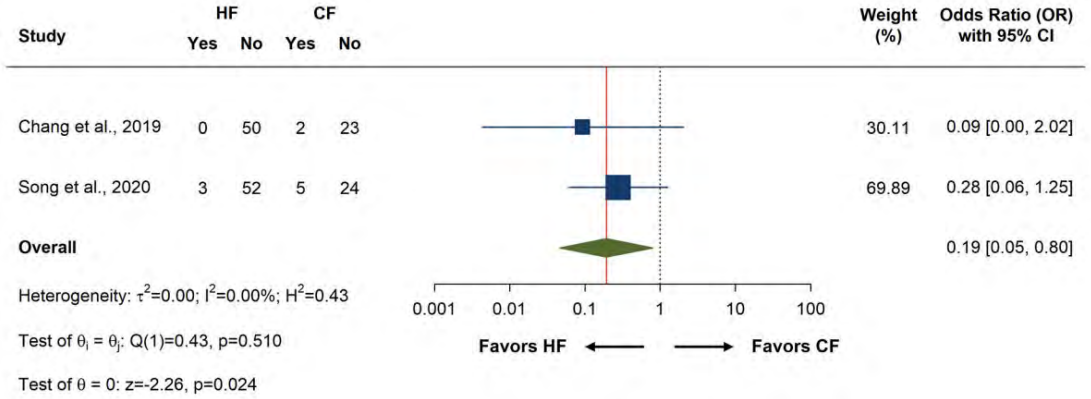

Fig. 3. Forest plot comparing incidence of major revisional surgery between HF and CF groups.

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En 2024

Etude RT CHARM (présentée à l'ASTRO 2024)

- Patients with pT0-2pN1-2 or pT3N0 or clinically staged prior to neoadjuvant chemotherapy (NAC) undergoing mastectomy with planned breast reconsctruction were randomized 1:1 to :
  - **Conventional PMRT :** 50 Gy in 25 fractions to the chest wall and/or reconstructed breast and regional nodes
  - **Hypofractionated PMRT :** 42,56 Gy in 16 fractions to the chest wall and/or reconstructed breast and regional nodes

- 898 patients from 209 sites in the US and Canada were enrolled from 2018-2021

- **Primary endpoint :**
  - Non-inferior reconstruction and complication rate at 24 months post-RT with hypofractionation
  - Non-inferiority margin of 10% assuming complication rate of 25% in the conventional arm

- Median follow-up 4,5 years

- **Results : Primary endpoint :**

  24 month incidence of complications 14,2% with hypofx vs 12,2 with conventional fractionation (p value <0,0004)

- Acute and late toxicity rates were not statistically different between arms

Take home message

- Schéma d'irradiation hypofractionné en cas de RMI par prothèse :
  - Tolérance équivalente
  - Efficacité non inférieure

- Tolérance différente entre expandeur et implant immédiat ?

- Besoin de données plus matures pour les jeunes patientes

- HYPOG-01 : hypofractionnement avec aires ganglionnaires => inclusion de patientes avec prothèse mammaire