

UNICANCER



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Ensemble, construisons l'avenir

NTCP en SRT

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Etat de l'art général

- ▶ suppose
 - ▶ la même sémantique
 - ▶ des pratiques de contourage des OAR standardisées
 - ▶ une échelle de cotation des toxicités validée et maîtrisée
 - ▶ un *reporting* harmonisé des surrogate markers (D, d, volume, endpoint clinique, f/u, risque estimé)
 - ▶ une irradiation homogène de l'OAR
- ▶ QUANTEC 2010 pour les domaines de doses conventionnelles (1,8-2,2 Gy/fr)

Etat de l'art en SRT

- ▶ données critiques ≠ : D_{max} (ponctuelle), dose sur faible volume
- ▶ modélisation dose-effet et calcul de dose isoE problématique
- ▶ techniques et modes de prescription différents
- ▶ suivi souvent <5 ans

- ▶ modélisation essentiellement sur données in vitro et modèles animaux (rongeurs, chiens)
- ▶ 1ères études RTOG spécifiques en 2002; nécessité d'un suivi > 5 ans
- ▶ données de tox émergentes parfois discordantes → guidelines topographiques basées sur 1 étude
- ▶ 1ère compilation en 2008 (Timmerman, *Semin Radiat Oncol*); nouvelle publi d'Emami en 2013, Grimm 2011 (1fr, 3 fr, 5 fr) : données essentiellement **non validées**
- plusieurs abaques dans chaque service !

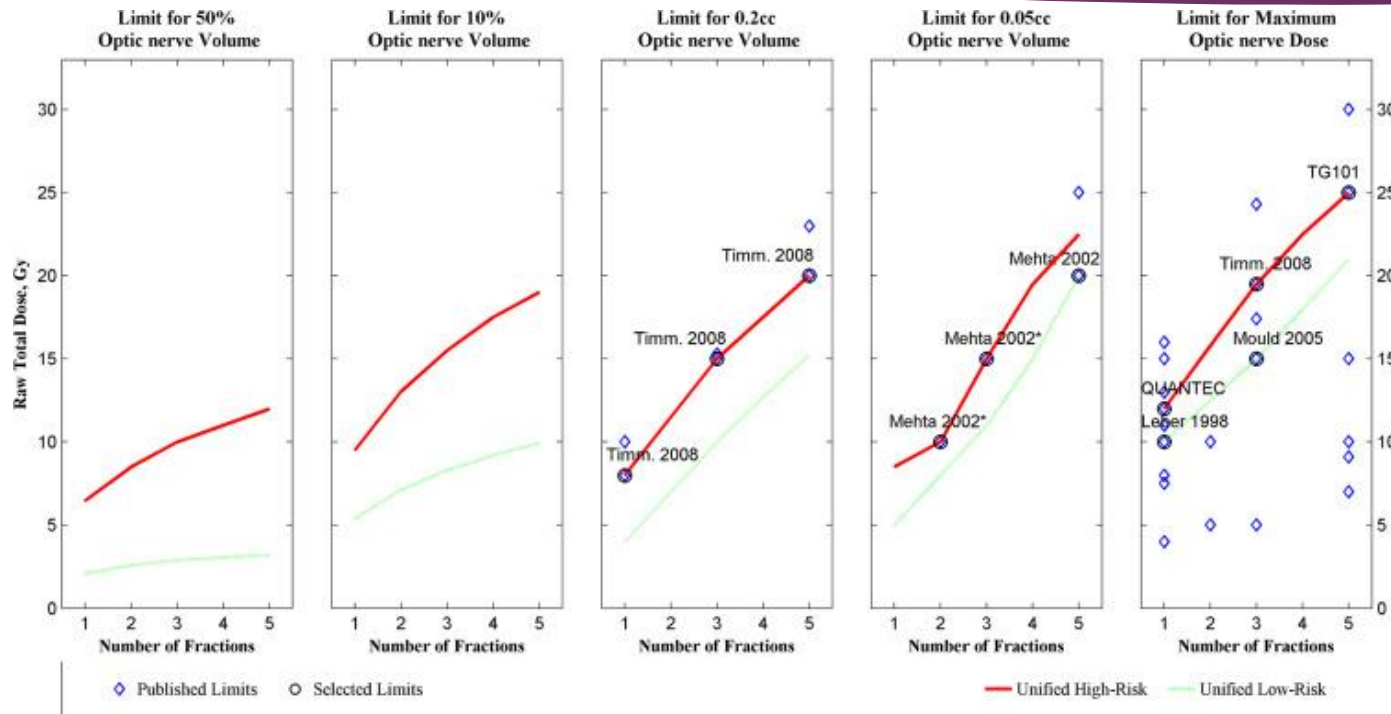
- ▶ *Estimates of NTCP are continually updated with every new publication containing toxicity estimates*
- développement d'une méthodologie originale : *DVH risk map*

DVH risk maps

courbe dose-effet avec :

- ▶ données publiées
- ▶ données institutionnelles
- ▶ pas de conversion de dose
- ▶ stratification en
 - ▶ faible risque d'événement (*cutoff* à 5% pour effets non létaux et 1% pour effets létaux)
 - ▶ fort risque (*cutoff* à 50% pour effets non létaux et 3% pour effets létaux)
- ▶ Qq exemples...

Voies optiques



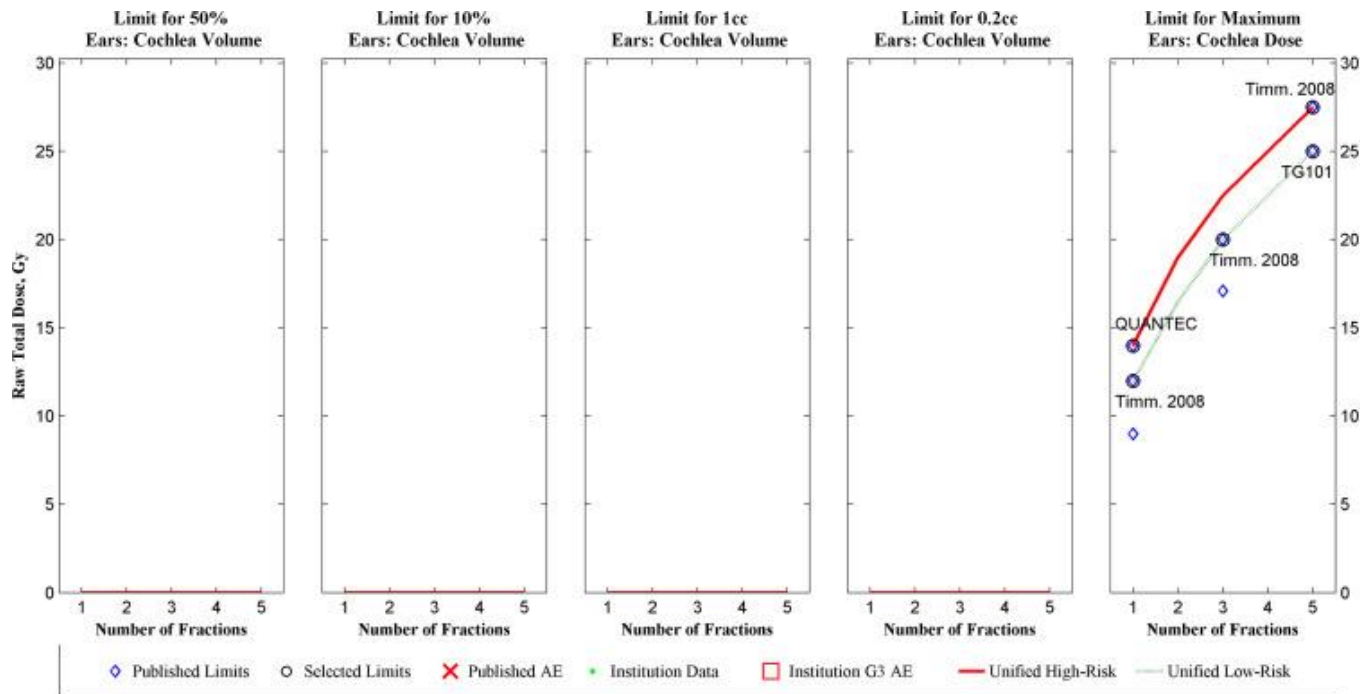
	Low Risk Limits					High Risk Limits				
	D50% Limit (Gy)	D10% Limit (Gy)	D0.2cc Limit (Gy)	D0.05cc Limit (Gy)	Dmax Limit (Gy)	D50% Limit (Gy)	D10% Limit (Gy)	D0.2cc Limit (Gy)	D0.05cc Limit (Gy)	Dmax Limit (Gy)
1 fx	2.1, 0.3%	5.4, 0.2%	4.0, 0.4%	5.0, 0.1%	10.0, 0.3%	6.5, 1.0%	9.5, 1.0%	8.0, 1.1%	8.5, 0.6%	12.0, 0.7%
2 fx	2.6, 0.3%	7.1, 0.2%	7.0, 0.6%	8.0, 0.2%	12.5, 0.2%	8.5, 1.0%	13.0, 1.0%	11.5, 1.2%	10.0, 0.4%	15.8, 0.6%
3 fx	2.9, 0.3%	8.3, 0.2%	10.0, 0.7%	11.0, 0.3%	15.0, 0.2%	10.0, 1.0%	15.5, 1.0%	15.0, 1.5%	15.0, 0.8%	19.5, 0.7%
4 fx	3.1, 0.3%	9.2, 0.2%	12.7, 0.9%	15.0, 0.6%	18.0, 0.3%	11.0, 1.0%	17.5, 1.0%	17.5, 1.6%	19.5, 1.4%	22.5, 0.8%
5 fx	3.2, 0.3%	9.9, 0.2%	15.2, 1.0%	20.0, 1.1%	21.0, 0.4%	12.0, 1.0%	19.0, 1.0%	20.0, 1.7%	22.5, 1.6%	25.0, 0.8%

Ccl des auteurs :

<1% incidence of RION if Dmax =

- 12 Gy in 1,
- 19.5 Gy in 3,
- and 25 Gy in 5 fractions.

Oreille interne



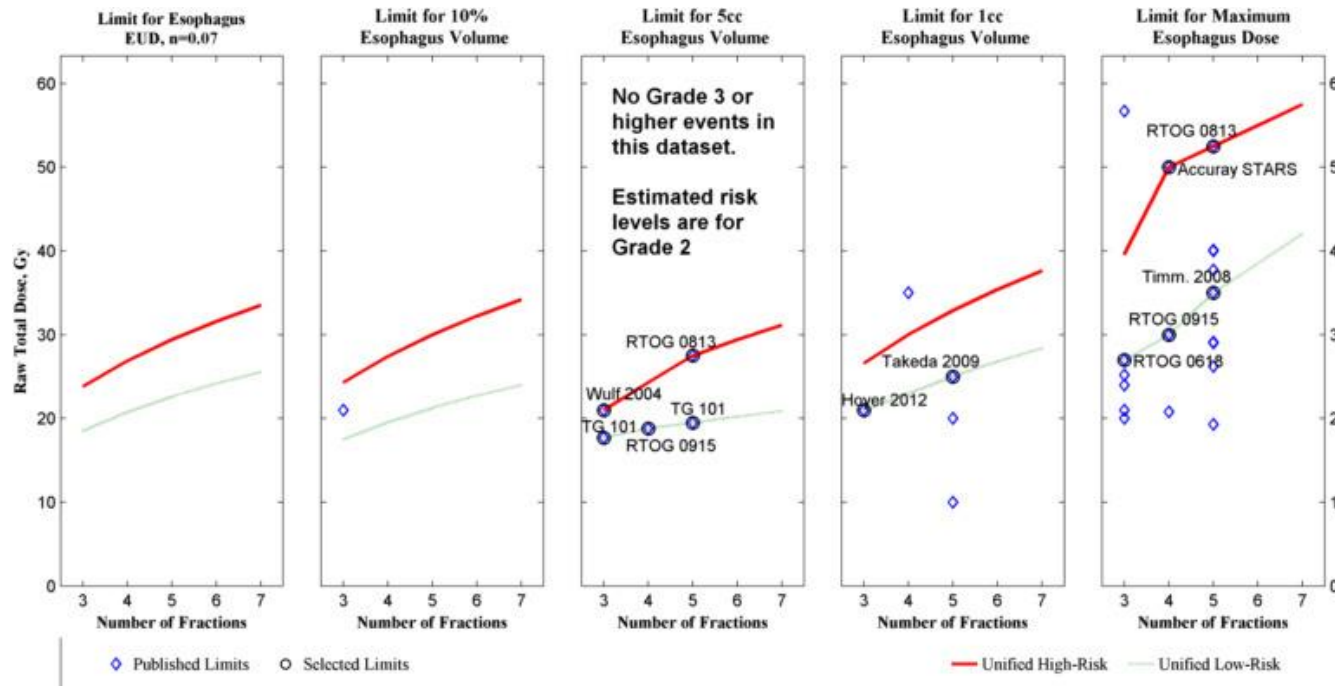
	Low Risk Limits					High Risk Limits				
	D50% Limit (Gy)	D10% Limit (Gy)	D1cc Limit (Gy)	D0.2cc Limit (Gy)	Dmax Limit (Gy)	D50% Limit (Gy)	D10% Limit (Gy)	D1cc Limit (Gy)	D0.2cc Limit (Gy)	Dmax Limit (Gy)
1 fx	-	-	-	-	12.0, 11.8%	-	-	-	-	14.0, 17.9%
2 fx	-	-	-	-	16.5, 12.4%	-	-	-	-	19.0, 17.9%
3 fx	-	-	-	-	20.0, 13.2%	-	-	-	-	22.5, 17.7%
4 fx	-	-	-	-	22.5, 13.2%	-	-	-	-	25.0, 17.2%
5 fx	-	-	-	-	25.0, 13.8%	-	-	-	-	27.5, 17.4%

Ccl des auteurs :

The 14 Gy in 1-fraction limit and the 27.5 Gy in 5-fraction limit had 17.9% and 17.4% risk, respectively.

For cases in which a lower risk is required, the 12 Gy in 1-fraction limit and the 25 Gy in 5-fraction limit had 11.8% and 13.8% risk, respectively.

Esophagus



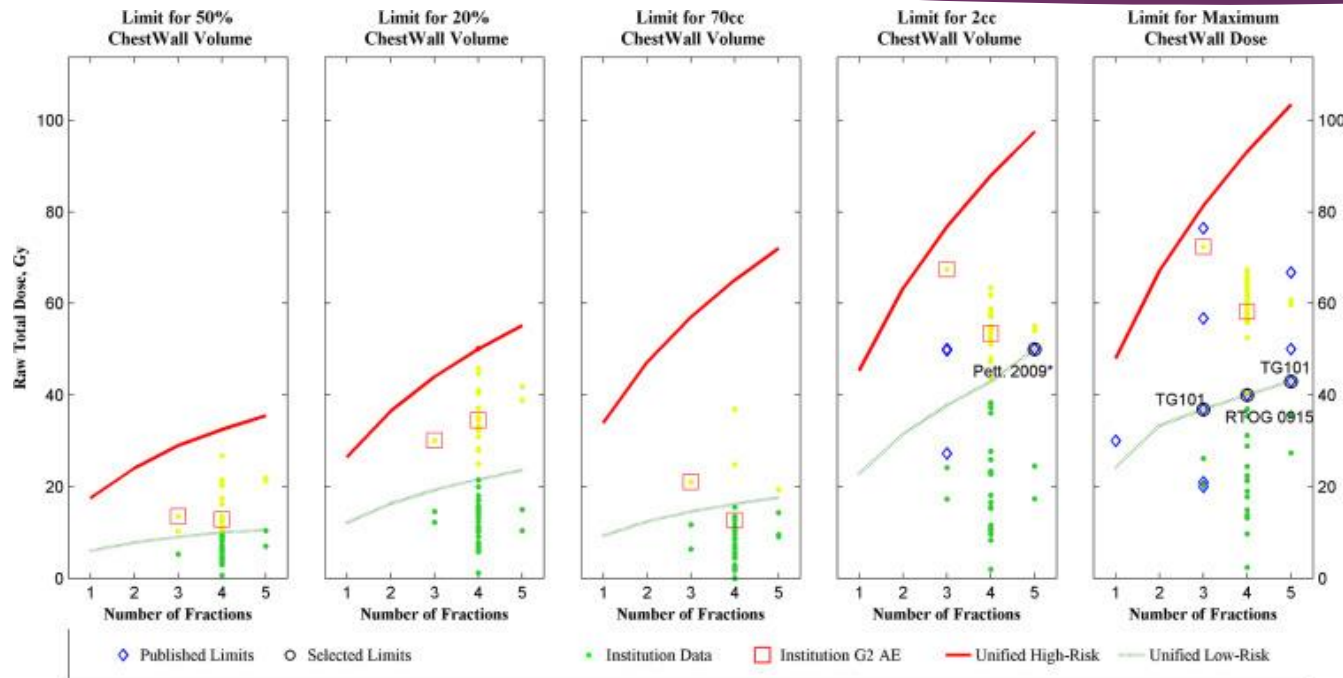
Ccl des auteurs :

$D_{1cc} = 32.9$ Gy ou $D_{max} 43,4$ Gy
 → 50% gr 2 tox

$D_{1cc} = 50.7$ Gy ou $D_{max} 61,4$ Gy
 → 50% gr 3 tox

	Low Risk Limits					High Risk Limits				
	EUD Limit (Gy)	D10% Limit (Gy)	D5cc Limit (Gy)	D1cc Limit (Gy)	Dmax Limit (Gy)	EUD Limit (Gy)	D10% Limit (Gy)	D5cc Limit (Gy)	D1cc Limit (Gy)	Dmax Limit (Gy)
3 fx	18.5, 5.0%	17.5, 5.0%	17.7, 19.7%	21.0, 6.9%	27.0, 6.3%	23.8, 50.0%	24.3, 50.0%	21.0, 40.6%	26.6, 50.0%	39.6, >50%
4 fx	20.8, 5.0%	19.6, 5.0%	18.8, 15.5%	23.0, 5.2%	30.0, 5.3%	26.9, 50.0%	27.4, 50.0%	24.3, 45.0%	30.0, 50.0%	50.0, >50%
5 fx	22.6, 5.0%	21.3, 5.0%	19.5, 12.5%	25.0, 5.0%	35.0, 9.8%	29.4, 50.0%	30.0, 50.0%	27.5, >50%	32.9, 50.0%	52.5, >50%
6 fx	24.2, 5.0%	22.7, 5.0%	20.2, 10.9%	26.8, 5.0%	38.5, 11.9%	31.6, 50.0%	32.2, 50.0%	29.4, 50.0%	35.4, 50.0%	55.0, >50%
7 fx	25.6, 5.0%	24.0, 5.0%	20.9, 10.0%	28.4, 5.0%	42.0, 15.0%	33.5, 50.0%	34.2, 50.0%	31.2, 50.0%	37.6, 50.0%	57.5, >50%

Côtes

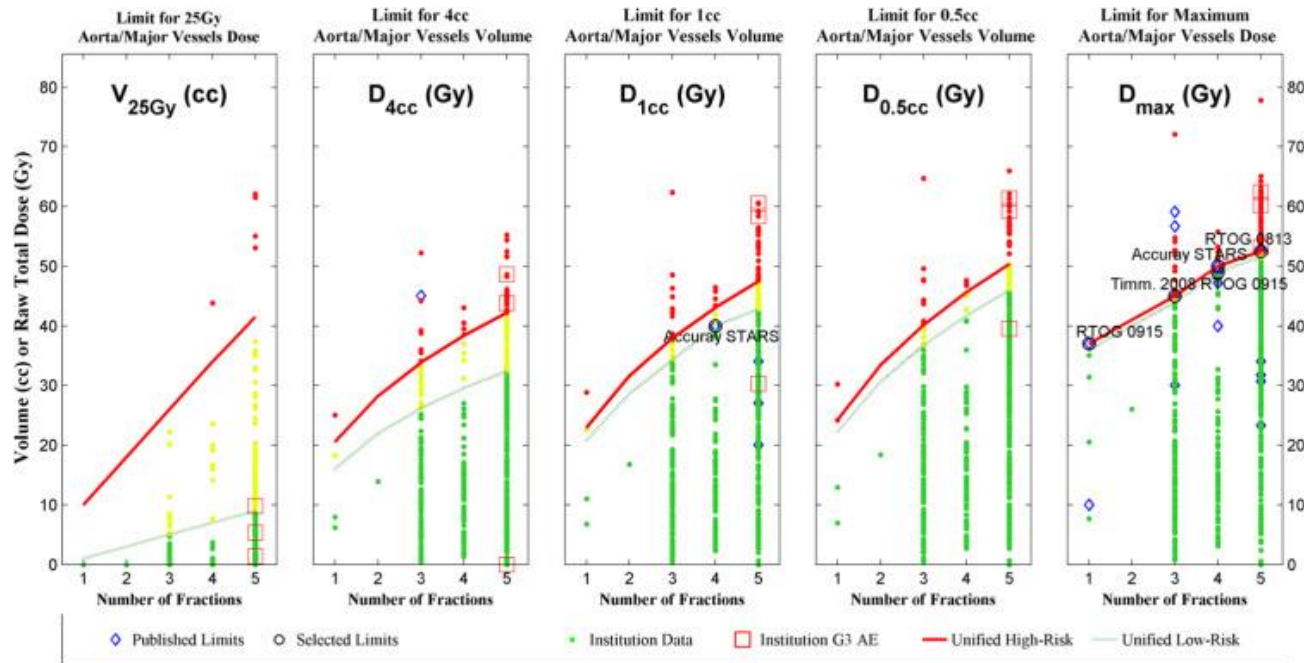


	Low Risk Limits					High Risk Limits				
	D50% Limit (Gy)	D20% Limit (Gy)	D70cc Limit (Gy)	D2cc Limit (Gy)	Dmax Limit (Gy)	D50% Limit (Gy)	D20% Limit (Gy)	D70cc Limit (Gy)	D2cc Limit (Gy)	Dmax Limit (Gy)
1 Fx	6.0	12.1	9.3, 10.0%	22.9, 10.0%	24.2, 10.0%	17.5	26.5	34.0, 50.0%	45.4, 50.0%	48.0, 50.0%
2 Fx	7.8	16.3	12.4, 10.0%	31.5, 10.0%	33.4, 10.0%	24.0	36.5	47.2, 50.0%	63.3, 50.0%	67.1, 50.0%
3 Fx	9.0	19.3	14.6, 10.0%	37.8, 10.0%	36.9, 8.4%	29.0	44.0	57.0, 50.0%	76.8, 50.0%	81.4, 50.0%
4 Fx	10.0	21.6	16.2, 10.0%	43.0, 10.0%	40.0, 7.6%	32.5	50.0	65.1, 50.0%	87.9, 50.0%	93.2, 50.0%
5 Fx	10.5	23.6	17.6, 10.0%	50.0, 11.2%	43.0, 7.3%	35.5	55.2	72.1, 50.0%	97.5, 50.0%	103.5, 50.0%

Ccl des auteurs :

The 10% risk level for grade 2 or higher complications for D_{70cc} was 16.2 Gy in 4 fractions, and the 50% risk level was $D_{70cc} = 65.1$ Gy in 4 fractions. For D_{2cc} , the 10% and 50% risk levels in 4 fractions were 43.0 Gy and 87.9 Gy, respectively.

Gros vaisseaux

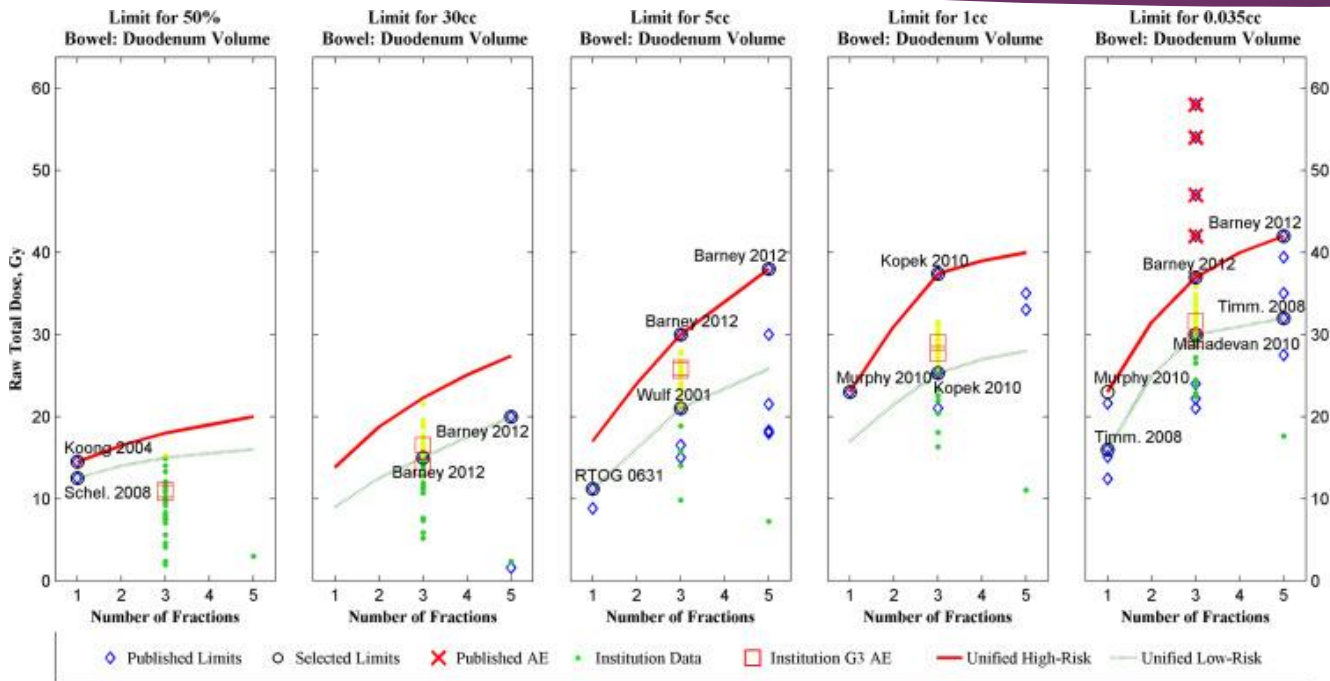


	Low Risk Limits					High Risk Limits				
	V25Gy Limit (cc)	D4cc Limit (Gy)	D1cc Limit (Gy)	D0.5cc Limit (Gy)	Dmax Limit (Gy)	V25Gy Limit (cc)	D4cc Limit (Gy)	D1cc Limit (Gy)	D0.5cc Limit (Gy)	Dmax Limit (Gy)
1 fx	1.0	16.1, 1.0%	20.8, 1.0%	22.2, 1.0%	36.0, 33.8%	10.0	20.5, 2.0%	22.9, 2.0%	24.2, 2.0%	37.0, 41.9%
2 fx	3.0	21.9, 1.0%	28.6, 1.0%	30.6, 1.0%	40.0, 4.2%	18.0	28.2, 2.0%	31.6, 2.0%	33.4, 2.0%	41.0, 5.3%
3 fx	5.0	26.2, 1.0%	34.3, 1.0%	36.8, 1.0%	44.0, 1.9%	26.0	33.8, 2.0%	37.9, 2.0%	40.2, 2.0%	45.0, 2.3%
4 fx	7.0	29.5, 1.0%	40.0, 1.2%	41.7, 1.0%	49.0, 1.5%	34.0	38.4, 2.0%	43.1, 2.0%	45.7, 2.0%	50.0, 1.8%
5 fx	9.0, 0.5%	32.4, 1.0%	42.8, 1.0%	46.0, 1.0%	51.5, 1.0%	41.5, 1.0%	42.2, 2.0%	47.5, 2.0%	50.4, 2.0%	52.5, 1.2%

Ccl des auteurs :

The RTOG 0813 dose-tolerance limit of $D_{max} = 52.5$ Gy in 5 fractions was found to have a 1.2% risk of grade 3-5 toxicity, and the Timmerman 2008 limit of $D_{max} = 45$ Gy in 3 fractions had 2.3% risk. From the model, the 1% and 2% risk levels for D_{4cc} , D_{1cc} , and $D_{0.5cc}$ were also provided

Duodénum



	Low Risk Limits					High Risk Limits				
	D50% Limit (Gy)	D30cc Limit (Gy)	D5cc Limit (Gy)	D1cc Limit (Gy)	D0.035cc Limit (Gy)	D50% Limit (Gy)	D30cc Limit (Gy)	D5cc Limit (Gy)	D1cc Limit (Gy)	D0.035cc Limit (Gy)
1 fx	12.5, 32.3%	9.0, 6.1%	11.2, 0.6%	17.0, 6.4%	16.0, 5.3%	14.5, 48.3%	13.8, 11.0%	17.0, 14.6%	23.0, 21.4%	23.0, 8.8%
2 fx	14.0, 19.3%	12.5, 6.3%	16.1, 0.9%	21.5, 4.9%	25.0, 6.2%	16.5, 30.2%	18.8, 11.0%	24.0, 18.8%	31.0, 19.5%	31.5, 8.7%
3 fx	15.0, 15.2%	15.0, 6.5%	21.0, 1.8%	25.3, 4.7%	30.0, 6.2%	18.0, 24.3%	22.3, 11.0%	30.0, 26.5%	37.4, 19.8%	37.0, 8.4%
4 fx	15.5, 12.7%	17.5, 6.8%	23.4, 1.7%	27.0, 3.9%	31.0, 5.6%	19.0, 20.9%	25.1, 11.0%	34.0, 26.8%	39.0, 14.2%	40.0, 7.8%
5 fx	16.0, 11.4%	20.0, 7.3%	25.8, 1.8%	28.0, 3.4%	32.0, 5.2%	20.0, 19.3%	27.4, 11.0%	38.0, 30.2%	40.0, 10.9%	42.0, 7.3%

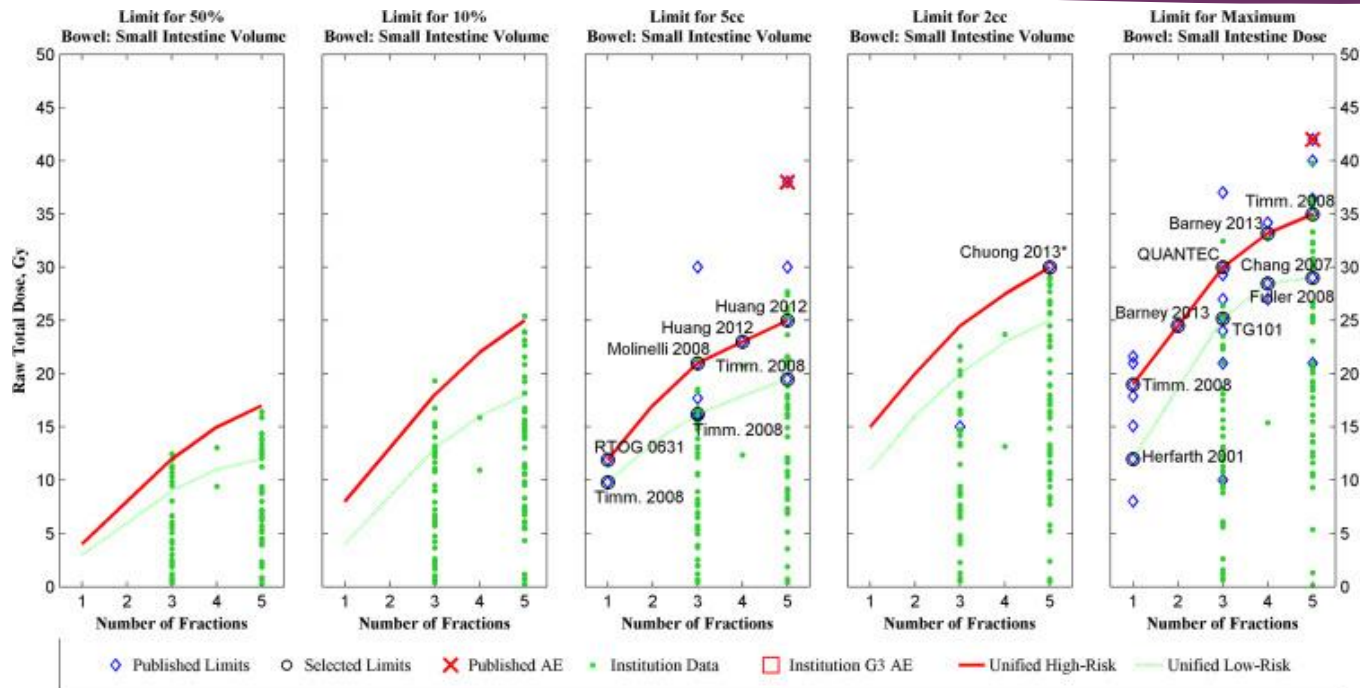
Ccl des auteurs :

low-risk limit of $D_{1cc} \leq 25.3$ Gy in 3 fr
 → risk of grade 3-4 duodenal complications of 4.7%

high-risk limit of $D_{1cc} \leq 37.4$ Gy in 3 fr
 → risk of Grade 3+ toxicity of 20%.

The 10% risk level, which is more clinically acceptable, was $D_{1cc} = 31.4$ Gy

Grêle



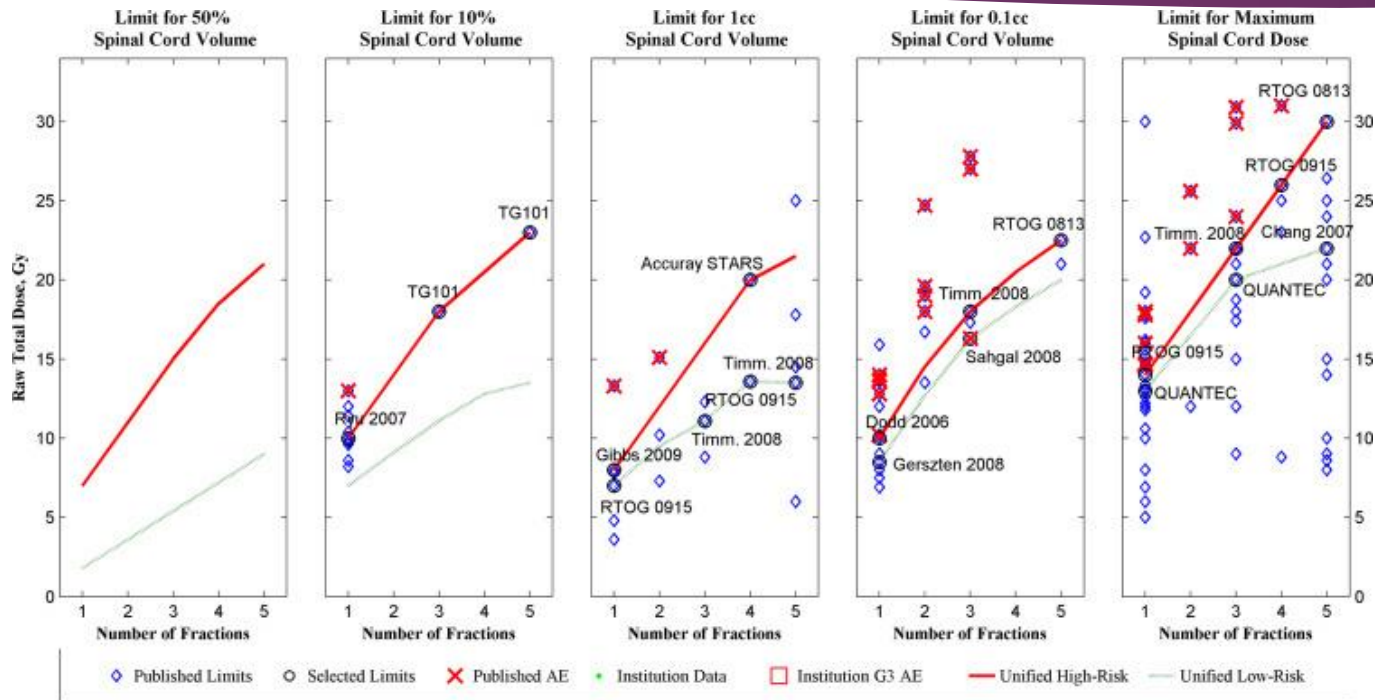
	Low Risk Limits					High Risk Limits				
	D50% Limit (Gy)	D10% Limit (Gy)	D5cc Limit (Gy)	D2cc Limit (Gy)	Dmax Limit (Gy)	D50% Limit (Gy)	D10% Limit (Gy)	D5cc Limit (Gy)	D2cc Limit (Gy)	Dmax Limit (Gy)
1 fx	3.0	4.0	9.8, 2.1%	11.0, 2.3%	12.0, 1.4%	4.0	8.0	11.9, 4.4%	15.0, 7.5%	19.0, 8.2%
2 fx	6.0	8.5	13.5, 2.3%	16.0, 3.0%	18.6, 2.3%	8.0	13.0	17.0, 5.5%	20.0, 6.9%	24.5, 6.4%
3 fx	9.0	13.0	16.2, 2.5%	20.0, 3.7%	25.2, 3.6%	12.0	18.0	21.0, 6.5%	24.5, 7.7%	30.0, 7.0%
4 fx	11.0	16.0	17.9, 2.4%	23.0, 4.0%	28.5, 3.7%	15.0	22.0	23.0, 5.9%	27.5, 7.6%	33.2, 6.5%
5 fx	12.0	18.0	19.5, 2.4%	25.0, 3.9%	29.0, 2.8%	17.0	25.0	25.0, 5.8%	30.0, 7.5%	35.0, 5.6%

Ccl des auteurs :

For low risk, $D_{5cc} = 16.2$ Gy in 3 fr \rightarrow 2.5% risk,

For high risk, $D_{5cc} = 21$ Gy in 3 fr \rightarrow 6.5% risk

Moelle



Ccl des auteurs :

We have presented estimates of risk for 18 commonly used dose tolerance limits in a unified format of high and low risk, to provide initial validation of current clinical practice.

	Low Risk Limits					High Risk Limits				
	D50% Limit (Gy)	D10% Limit (Gy)	D1cc Limit (Gy)	D0.1cc Limit (Gy)	Dmax Limit (Gy)	D50% Limit (Gy)	D10% Limit (Gy)	D1cc Limit (Gy)	D0.1cc Limit (Gy)	Dmax Limit (Gy)
1 fx	1.8	7.0	7.0, 0.1%	8.5, 0.1%	13.0, 0.9%	7.0	10.0	8.0, 0.2%	10.0, 0.2%	14.0, 1.6%
2 fx	3.6	9.1	9.5, 0.1%	12.7, 0.1%	16.5, 0.6%	11.0	14.0	12.0, 0.4%	14.5, 0.3%	18.0, 1.1%
3 fx	5.4	11.1	11.1, 0.1%	16.3, 0.2%	20.0, 0.7%	15.0	18.0	16.0, 0.9%	18.0, 0.4%	22.0, 1.3%
4 fx	7.2	12.8	13.6, 0.2%	18.3, 0.2%	21.0, 0.5%	18.5	20.5	20.0, 2.2%	20.5, 0.4%	26.0, 1.8%
5 fx	9.0	13.5	13.5, 0.1%	20.0, 0.2%	22.0, 0.4%	21.0	23.0	21.5, 2.0%	22.5, 0.4%	30.0, 2.6%