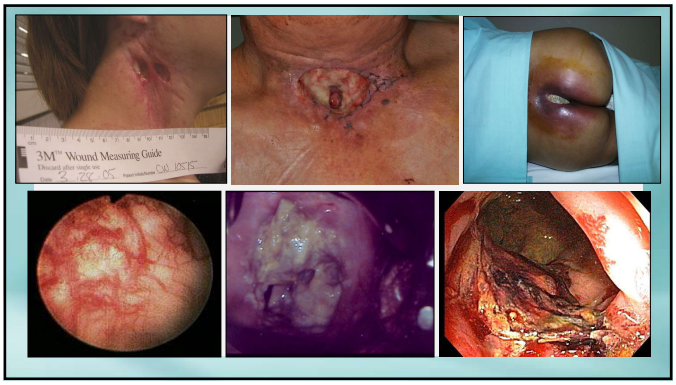
Radiation-Induced Soft Tissue Injuries

Hyperbaric Oxygen as Standard of Care?

Primary Training in Hyperbaric Medicine
Columbia, South Carolina



Radiation Tissue Injury: "Non-Target" Tissues

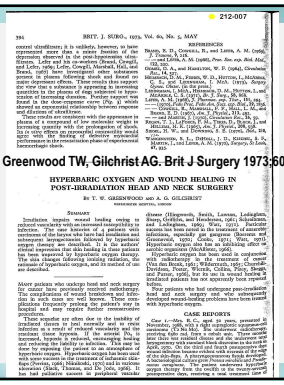
Acute effects: *mucosa, other rapidly proliferating cells*

usually benign +/- RT pause

Late effects: *chronic oxidative stress*

dose-dependent

complex wounds/organ loss



212-007

BRIT. J. SURG., 1973, Vol. 60, No. 5, MAY

REFERENCES

HYPERBARIC OXYGEN AND WOUND HEALING IN POST-IRRADIATION HEAD AND NECK SURGERY

BY T. W. GREENWOOD AND A. G. GILCHRIST

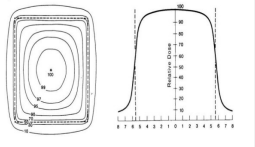
SUMMARY

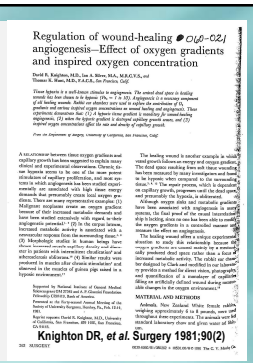
CASE REPORTS

Greenwood TW, Gilchrist AG. Brit J Surgery 1973;60(5)

BEAM PROFILE

The dose variation across the field at a specified depth.





Regulation of wound-healing angiogenesis—Effect of oxygen gradients and inspired oxygen concentration

David S. Knighton, M.D., Ian A. Silver, M.A., M.R.C.V.S., and Thomas K. Hunt, M.D., F.A.C.S., *San Francisco, Calif.*

Knighton DR, *et al.* Surgery 1981;90(2)

Evolution of radiation-induced soft tissue injuries

Some minor symptoms resolve spontaneously
others with conservative care

Remitting-relapsing characteristics

Other seemingly minor symptoms prove refractory
disease progression despite "standard" care

New forms of injury may evolve > advanced care
leading in some cases to loss of organ or death

Rectal RT injury complex

- Microscopic hemorrhage
- Macroscopic hemorrhage
- Mucosal loss
- Pain/tenesmus
- Frequency
- Loss of sphincter control
- Stricture
- Ulceration
- Death

HYPERBARIC OXYGEN TREATMENT OF CHRONIC RADIATION PROCTITIS: A RANDOMIZED AND CONTROLLED DOUBLE-BLIND CROSSOVER TRIAL WITH LONG-TERM FOLLOW-UP

Clarke RE, *et al.* Int. J Rad Oncol Biol Phys 2008;72

Trial design

226 screened for eligibility

150 enrolled/randomized (1:1)
66% ratio

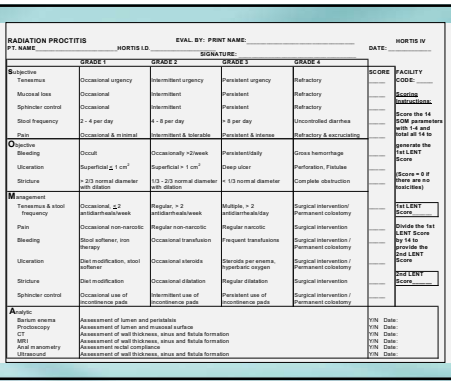
120 evaluable
64 HBO 2.0 ATA O2
56 Sham 1.3 > 1.0 ATA air

Objective & subjective criteria

HBO higher response rates
SOMA p=0.0019
clinical assessment p=0.0009
bowel bother
bowel function

All differences abolished at cross-over

Elimination of remitting/relapsing sequence
"disease modification"



RADIATION PROCTITIS
PT. NAME:_____ HORTIS I.D. _____
EVAL. BY: PRINT NAME:_____
SIGNATURE:
HORTIS IV
DATE:_____

	GRADE 1	GRADE 2	GRADE 3	GRADE 4	SCORE
Subjective					
Tenesmus	Occasional urgency	Intermittent urgency	Persistent urgency	Refractory	____
Mucosal loss	Occasional	Intermittent	Persistent	Refractory	____
Sphincter control	Occasional	Intermittent	Persistent	Refractory	____
Stool frequency	2 - 4 per day	4 - 8 per day	> 8 per day	Uncontrolled diarrhea	____
Pain	Occasional & minimal	Intermittent & tolerable	Persistent & intense	Refractory & excruciating	____
Objective					
Bleeding	Occult	Occasionally >2/week	Persistent/daily	Gross hemorrhage	____
Ulceration	Superficial ≤ 1 cm²	Superficial > 1 cm²	Deep ulcer	Perforation, Fistulae	____
Stricture	> 2/3 normal diameter with dilation	1/3 - 2/3 normal diameter with dilation	< 1/3 normal diameter	Complete obstruction	____
Management					
Tenesmus & stool frequency	Occasional, ≤ 2 antidiarrheals/week	Regular, > 2 antidiarrheals/week	Multiple, > 2 antidiarrheals/day	Surgical intervention/ Permanent colostomy	1st LENT Score_____
Pain	Occasional non-narcotic	Regular non-narcotic	Regular narcotic	Surgical intervention	
Bleeding	Stool softener, iron therapy	Occasional transfusion	Frequent transfusions	Surgical intervention / Permanent colostomy	
Ulceration	Diet modification, stool softener	Occasional steroids	Steroids per enema, hyperbaric oxygen	Surgical intervention / Permanent colostomy	2nd LENT Score_____
Stricture	Diet modification	Occasional dilatation	Regular dilatation	Surgical intervention	
Sphincter control	Occasional use of incontinence pads	Intermittent use of incontinence pads	Persistent use of incontinence pads	Surgical intervention / Permanent colostomy	
Analytic					
Barium enema	Assessment of lumen and peristalsis				Y/N Date:
Proctoscopy	Assessment of lumen and mucosal surface				Y/N Date:
CT	Assessment of wall thickness, sinus and fistula formation				Y/N Date:
MRI	Assessment of wall thickness, sinus and fistula formation				Y/N Date:
Anal manometry	Assessment rectal compliance				Y/N Date:
Ultrasound	Assessment of wall thickness, sinus and fistula formation				Y/N Date:

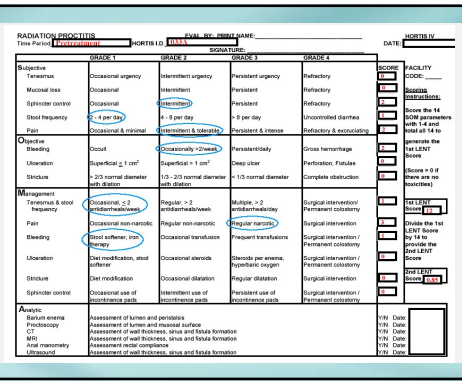
FACILITY CODE: _____

Scoring Instructions:

Score the 14 SOM parameters with 1-4 and total all 14 to generate the 1st LENT Score

(Score = 0 if there are no toxicities)

Divide the 1st LENT Score by 14 to provide the 2nd LENT Score



RADIATION PROCTITIS
Time Period: Pretreatment HORTIS I.D. 0033
EVAL. BY: PRINT NAME:_____
SIGNATURE:
HORTIS IV
DATE:_____

	GRADE 1	GRADE 2	GRADE 3	GRADE 4	SCORE
Subjective					
Tenesmus	Occasional urgency	Intermittent urgency	Persistent urgency	Refractory	1
Mucosal loss	Occasional	Intermittent	Persistent	Refractory	1
Sphincter control	Occasional	Intermittent	Persistent	Refractory	1
Stool frequency	2 - 4 per day	4 - 8 per day	> 8 per day	Uncontrolled diarrhea	1
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Scoring Instructions:

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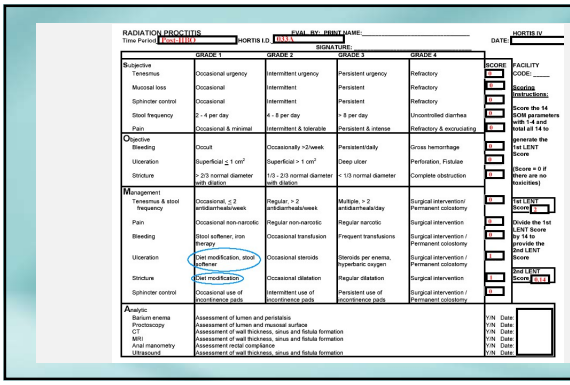
(Score = 0 if there are no toxicities)

Divide the 1st LENT Score by 14 to provide the 2nd LENT Score

1st LENT Score 11

2nd LENT Score 0.79



RADIATION PROCTITIS
Time Period: 6 mos HORTIS I.D. 0033
EVAL. BY: PRINT NAME:_____
SIGNATURE:
HORTIS IV
DATE:_____

	GRADE 1	GRADE 2	GRADE 3	GRADE 4	SCORE
Subjective					
Tenesmus	Occasional urgency	Intermittent urgency	Persistent urgency	Refractory	1
Mucosal loss	Occasional	Intermittent	Persistent	Refractory	1
Sphincter control	Occasional	Intermittent	Persistent	Refractory	1
Stool frequency	2 - 4 per day	4 - 8 per day	> 8 per day	Uncontrolled diarrhea	1
Pain	Occasional & minimal	Intermittent & tolerable	Persistent & intense	Refractory & excruciating	1
Objective					
Bleeding	Occult	Occasionally >2/week	Persistent/daily	Gross hemorrhage	1
Ulceration	Superficial ≤ 1 cm²	Superficial > 1 cm²	Deep ulcer	Perforation, Fistulae	1
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Tenesmus & stool frequency	Occasional, ≤ 2 antidiarrheals/week	Regular, > 2 antidiarrheals/week	Multiple, > 2 antidiarrheals/day	Surgical intervention/ Permanent colostomy	1
Pain	Occasional non-narcotic	Regular non-narcotic	Regular narcotic	Surgical intervention	1
Bleeding	Stool softener, iron therapy	Occasional transfusion	Frequent transfusions	Surgical intervention / Permanent colostomy	1
Ulceration	Diet modification, stool softener	Occasional steroids	Steroids per enema, hyperbaric oxygen	Surgical intervention / Permanent colostomy	1
Stricture	Diet modification	Occasional dilatation	Regular dilatation	Surgical intervention	1
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CT	Assessment of wall thickness, sinus and fistula formation				Y/N Date:
MRI	Assessment of wall thickness, sinus and fistula formation				Y/N Date:
Anal manometry	Assessment rectal compliance				Y/N Date:
Ultrasound	Assessment of wall thickness, sinus and fistula formation				Y/N Date:

FACILITY CODE: _____

Scoring Instructions:

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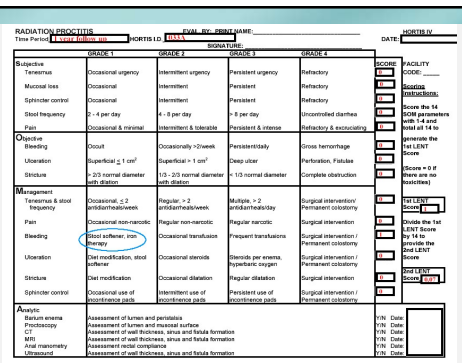
(Score = 0 if there are no toxicities)

Divide the 1st LENT Score by 14 to provide the 2nd LENT Score

1st LENT Score 11

2nd LENT Score 0.79



RADIATION PROCTITIS
Time Period: 1 year follow up HORTIS I.D. 0033
EVAL. BY: PRINT NAME:_____
SIGNATURE:
HORTIS IV
DATE:_____

	GRADE 1	GRADE 2	GRADE 3	GRADE 4	SCORE
Subjective					
Tenesmus	Occasional urgency	Intermittent urgency	Persistent urgency	Refractory	1
Mucosal loss	Occasional	Intermittent	Persistent	Refractory	1
Sphincter control	Occasional	Intermittent	Persistent	Refractory	1
Stool frequency	2 - 4 per day	4 - 8 per day	> 8 per day	Uncontrolled diarrhea	1
Pain	Occasional & minimal	Intermittent & tolerable	Persistent & intense	Refractory & excruciating	1
Objective					
Bleeding	Occult	Occasionally >2/week	Persistent/daily	Gross hemorrhage	1
Ulceration	Superficial ≤ 1 cm²	Superficial > 1 cm²	Deep ulcer	Perforation, Fistulae	1
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Pain	Occasional non-narcotic	Regular non-narcotic	Regular narcotic	Surgical intervention	1
Bleeding	Stool softener, iron therapy	Occasional transfusion	Frequent transfusions	Surgical intervention / Permanent colostomy	1
Ulceration	Diet modification, stool softener	Occasional steroids	Steroids per enema, hyperbaric oxygen	Surgical intervention / Permanent colostomy	1
Stricture	Diet modification	Occasional dilatation	Regular dilatation	Surgical intervention	1
Sphincter control	Occasional use of incontinence pads	Intermittent use of incontinence pads	Persistent use of incontinence pads	Surgical intervention / Permanent colostomy	1
Analytic					
Barium enema	Assessment of lumen and peristalsis				Y/N Date:
Proctoscopy	Assessment of lumen and mucosal surface				Y/N Date:
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MRI	Assessment of wall thickness, sinus and fistula formation				Y/N Date:
Anal manometry	Assessment rectal compliance				Y/N Date:
Ultrasound	Assessment of wall thickness, sinus and fistula formation				Y/N Date:

FACILITY CODE: _____

Scoring Instructions:

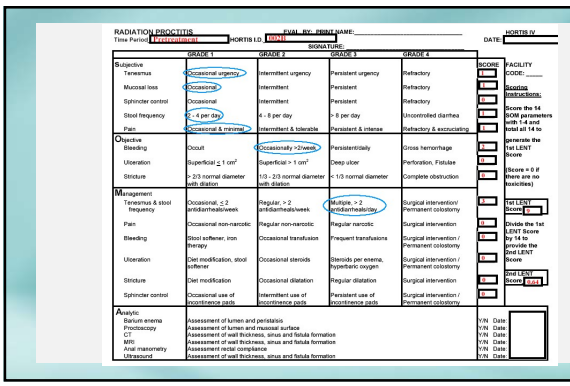
Score the 14 SOM parameters with 1-4 and total all 14 to generate the 1st LENT Score

(Score = 0 if there are no toxicities)

Divide the 1st LENT Score by 14 to provide the 2nd LENT Score

1st LENT Score 11

2nd LENT Score 0.79



RADIATION PROCTITIS
Time Period: Pretreatment HORTIS I.D. 0026
EVAL. BY: PRINT NAME:_____
SIGNATURE:
HORTIS IV
DATE:_____

	GRADE 1	GRADE 2	GRADE 3	GRADE 4	SCORE
Subjective					
Tenesmus	Occasional urgency	Intermittent urgency	Persistent urgency	Refractory	1
Mucosal loss	Occasional	Intermittent	Persistent	Refractory	1
Sphincter control	Occasional	Intermittent	Persistent	Refractory	1
Stool frequency	2 - 4 per day	4 - 8 per day	> 8 per day	Uncontrolled diarrhea	1
Pain	Occasional & minimal	Intermittent & tolerable	Persistent & intense	Refractory & excruciating	1
Objective					
Bleeding	Occult	Occasionally >2/week	Persistent/daily	Gross hemorrhage	1
Ulceration	Superficial ≤ 1 cm²	Superficial > 1 cm²	Deep ulcer	Perforation, Fistulae	1
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Pain	Occasional non-narcotic	Regular non-narcotic	Regular narcotic	Surgical intervention	1
Bleeding	Stool softener, iron therapy	Occasional transfusion	Frequent transfusions	Surgical intervention / Permanent colostomy	1
Ulceration	Diet modification, stool softener	Occasional steroids	Steroids per enema, hyperbaric oxygen	Surgical intervention / Permanent colostomy	1
Stricture	Diet modification	Occasional dilatation	Regular dilatation	Surgical intervention	1
Sphincter control	Occasional use of incontinence pads	Intermittent use of incontinence pads	Persistent use of incontinence pads	Surgical intervention / Permanent colostomy	1
Analytic					
Barium enema	Assessment of lumen and peristalsis				Y/N Date:
Proctoscopy	Assessment of lumen and mucosal surface				Y/N Date:
CT	Assessment of wall thickness, sinus and fistula formation				Y/N Date:
MRI	Assessment of wall thickness, sinus and fistula formation				Y/N Date:
Anal manometry	Assessment rectal compliance				Y/N Date:
Ultrasound	Assessment of wall thickness, sinus and fistula formation				Y/N Date:

FACILITY CODE: _____

Scoring Instructions:

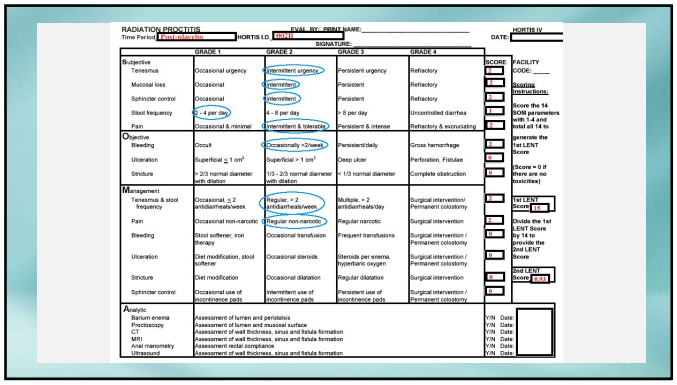
Score the 14 SOM parameters with 1-4 and total all 14 to generate the 1st LENT Score

(Score = 0 if there are no toxicities)

Divide the 1st LENT Score by 14 to provide the 2nd LENT Score

1st LENT Score 11

2nd LENT Score 0.64


RADIATION PROCTITIS
Time Period: Pre-HBOT
HORTIS I.D.: HBOT
EVAL. BY: PRINT NAME:
SIGNATURE:
DATE:
HORTIS IV

	GRADE 1	GRADE 2	GRADE 3	GRADE 4	SCORE
Subjective					
Tenesmus	Occasional urgency	Intermittent urgency	Persistent urgency	Refractory	
Mucosal loss	Occasional	Intermittent	Persistent	Refractory	
Sphincter control	Occasional	Intermittent	Persistent	Refractory	
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Objective					
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MRI	Assessment of wall thickness, sinus and fistula formation				Y/N Date:
Anal manometry	Assessment rectal compliance				Y/N Date:
Ultrasound	Assessment of wall thickness, sinus and fistula formation				Y/N Date:

FACILITY CODE:

Scoring Instructions:

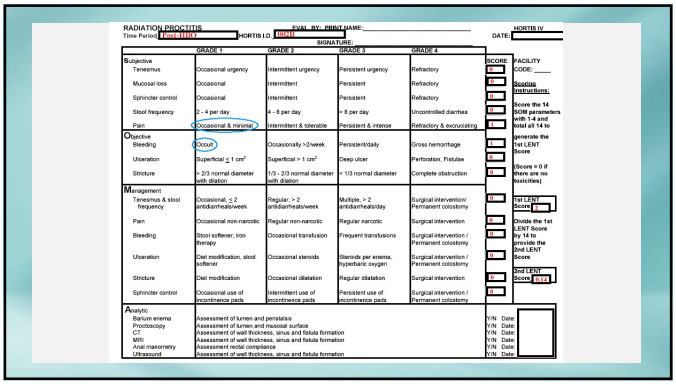
Score the 14 SOM parameters with 1-4 and total all 14 to generate the 1st LENT Score

(Score = 0 if there are no toxicities)

1st LENT Score:

Divide the 1st LENT Score by 14 to provide the 2nd LENT Score

2nd LENT Score:


RADIATION PROCTITIS
Time Period: Post-HBOT
HORTIS I.D.: HBOT
EVAL. BY: PRINT NAME:
SIGNATURE:
DATE:
HORTIS IV

	GRADE 1	GRADE 2	GRADE 3	GRADE 4	SCORE
Subjective					
Tenesmus	Occasional urgency	Intermittent urgency	Persistent urgency	Refractory	
Mucosal loss	Occasional	Intermittent	Persistent	Refractory	
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FACILITY CODE:

Scoring Instructions:

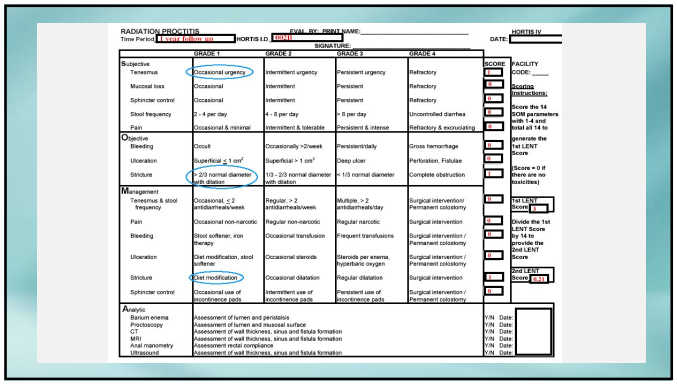
Score the 14 SOM parameters with 1-4 and total all 14 to generate the 1st LENT Score

(Score = 0 if there are no toxicities)

1st LENT Score:

Divide the 1st LENT Score by 14 to provide the 2nd LENT Score

2nd LENT Score:


RADIATION PROCTITIS
Time Period: 1 Year Follow-up
HORTIS I.D.: HBOT
EVAL. BY: PRINT NAME:
SIGNATURE:
DATE:
HORTIS IV

	GRADE 1	GRADE 2	GRADE 3	GRADE 4	SCORE
Subjective					
Tenesmus	Occasional urgency	Intermittent urgency	Persistent urgency	Refractory	
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Sphincter control	Occasional use of incontinence pads	Intermittent use of incontinence pads	Persistent use of incontinence pads	Surgical intervention / Permanent colostomy	
Analytic					
Barium enema	Assessment of lumen and peristalsis				Y/N Date:
Proctoscopy	Assessment of lumen and mucosal surface				Y/N Date:
CT	Assessment of wall thickness, sinus and fistula formation				Y/N Date:
MRI	Assessment of wall thickness, sinus and fistula formation				Y/N Date:
Anal manometry	Assessment rectal compliance				Y/N Date:
Ultrasound	Assessment of wall thickness, sinus and fistula formation				Y/N Date:

FACILITY CODE:

Scoring Instructions:

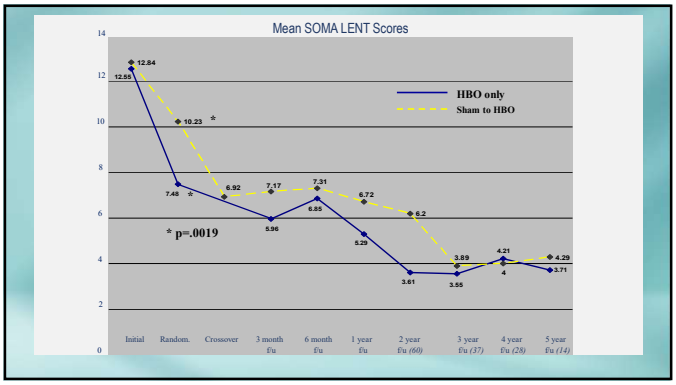
Score the 14 SOM parameters with 1-4 and total all 14 to generate the 1st LENT Score

(Score = 0 if there are no toxicities)

1st LENT Score: 9

Divide the 1st LENT Score by 14 to provide the 2nd LENT Score

2nd LENT Score: 0.71



LENT score reduction; clinical implications

Pre-treatment LENT score of 13

deep ulceration; intermittent pain; bleeding (>2 weekly); treated with regular non-narcotic, occasional transfusions & steroids

Post-treatment LENT score of 7

occasional pain, occult bleeding; occasional urgency; treated with anti-diarrheals; occasional non-narcotics, stool softeners, diet modification

1 year follow-up LENT score of 5

occasional pain, treated with occasional non-narcotic; stool softener; diet modification & iron therapy

Patient beliefs (blinding)

72 pts. asked what they thought their randomization was

	HBO	Sham	Don't Know
HBO Group (33)	20	1	12
Sham Group (39)	23	2	14

Chi-square test detects no relationship (p =0.9058)

Ignoring those who did not know, Kappa statistic p=0.0299

Harms

Ear barotrauma

19 pts (15.8%) complained of ear pain/discomfort
- *11 unremarkable exam*
- *7 TM changes only*
- *1 TM change & middle ear effusion*

decongestants…8 ventilation tubes…7 no tx…4

Sinus barotrauma

1 pt. (0.08%), tx. with decongestants

Transient myopia

4 pts. (3.3%)

Confinement anxiety

2 pts. (1.7%) sedative…1 reassurance…1

Treatment failure

Local recurrence vs. residual tumor as failed clinical response/relapse risk

45% (3) of those who failed to respond per SOMA dx with cancer

SOMA scores in pts who either failed to respond or improved then relapsed > by average of 9 (4-7) at f/u when CA dx.


Articles

Hyperbaric oxygen for patients with chronic bowel dysfunction after pelvic radiotherapy (HOT2): a randomised, double-blind, sham-controlled phase 3 trial

Glover M, *et al.* Lancet Oncology 2016;17(2):224-233

Trial design

241 screened for eligibility

84 enrolled/randomized (2:1)
35%

Reported
- *40 HBO 2.4 ATA O2 per mask*
- *25 Sham 1.3 ATA air per mask*

Subjective primary endpoint
- *change in IBD questionnaire score*
- *IBDQ rectal bleeding score at 1 yr*


Correspondence

216-087

Hyperbaric oxygen therapy for chronic bowel dysfunction after pelvic radiotherapy

"This trial is VERY upsetting!

We have seen such consistently good results in the patients treated off trial, in terms of healing ulceration & treating bleeding - in fact, there is no one in 10 years who has not responded well to HBO.

I must have sent 4 or 5 a year - and it is very difficult to understand our trial results'"


216-103

Clinical Case Study

The Effect of Hyperbaric Oxygen Therapy on Rectal Ulcers after Argon Plasma Coagulation

Ana Laranjo Maria Carvalho Andreia Fiel Nuno Veloso Isabel Medeiros

Laranjo A, *et al.* Port J Gastroenterology 2020;Oct

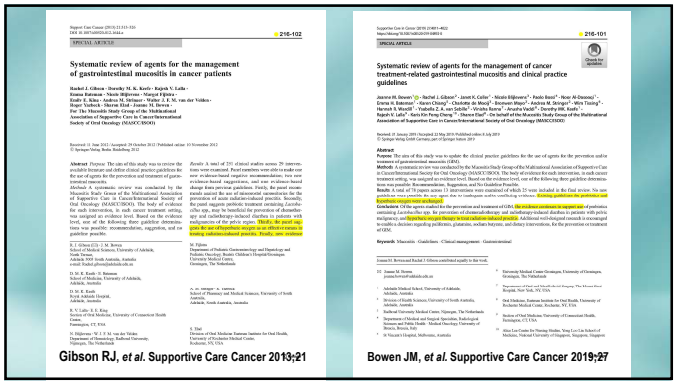
Radiation proctitis

Post APC

10 mm ulcer at site of APC

Rectal ulcer after HBO x 20

Healed after HBO x 50

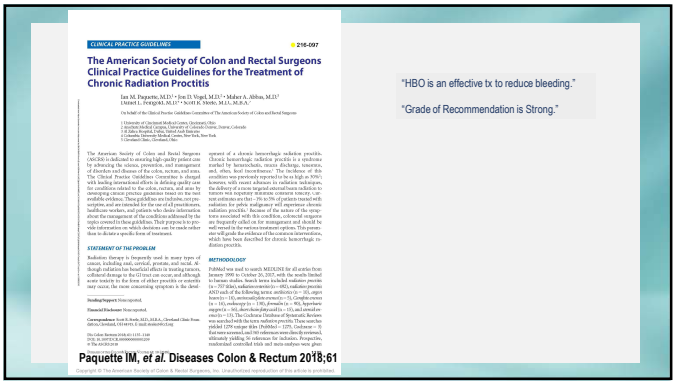


Systematic review of agents for the management of gastrointestinal mucositis in cancer patients

Gibson RJ, *et al.* Supportive Care Cancer 2013;21

Systematic review of agents for the management of cancer treatment-related gastrointestinal mucositis and clinical practice guidelines

Bowen JM, *et al.* Supportive Care Cancer 2019;27



The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for the Treatment of Chronic Radiation Proctitis

"HBO is an effective tx to reduce bleeding."

"Grade of Recommendation is Strong."

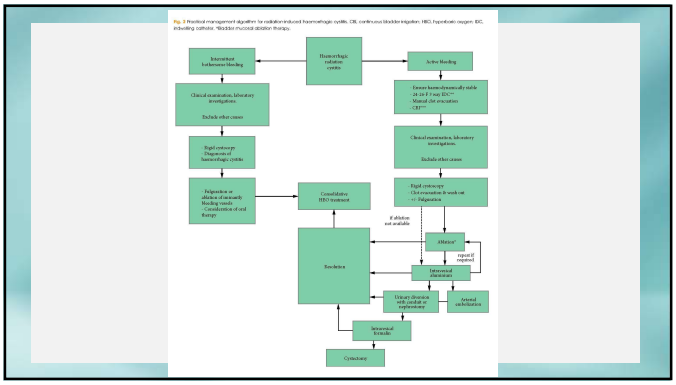
Paquette IM, *et al.* Diseases Colon & Rectum 2018;61

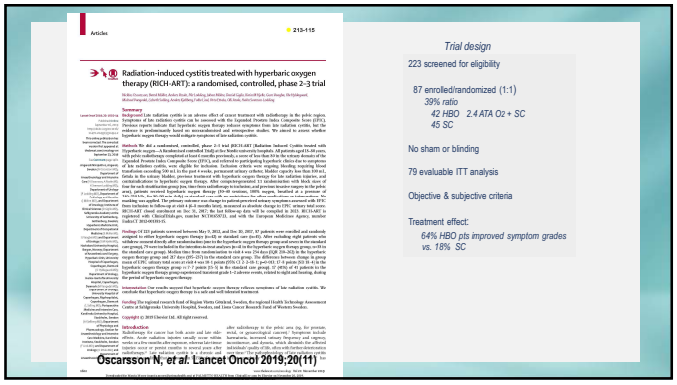
Current management of radiation cystitis: a review and practical guide to clinical management

Injury complex

- Dysuria/incontinence
- Frequency/urgency
- Pain
- Inflammation
- Vascular telangiectasis
- Bullous erythema
- Microscopic hemorrhage
- Macroscopic hemorrhage
- Clot retention/obstruction
- Reduced bladder capacity
- Hemorrhagic ulceration
- Loss of mucosal integrity
- Urethral stricture/fibrosis
- Bladder neck contracture
- Tissue necrosis
- Vesico-vaginal fistula
- Colo-vesical fistula
- Ulceration/rupture

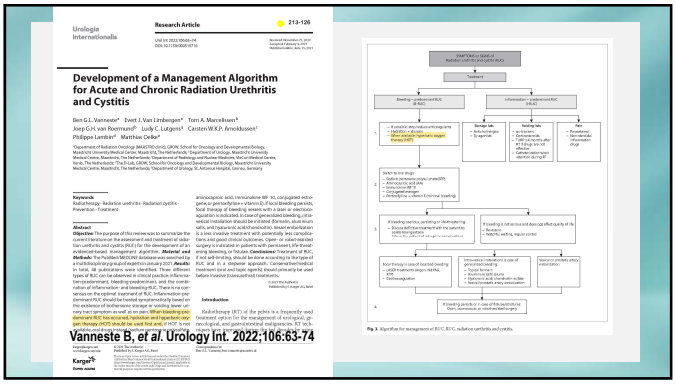
Pascoe C, *et al.* Brit J Urology Int. 2019;123





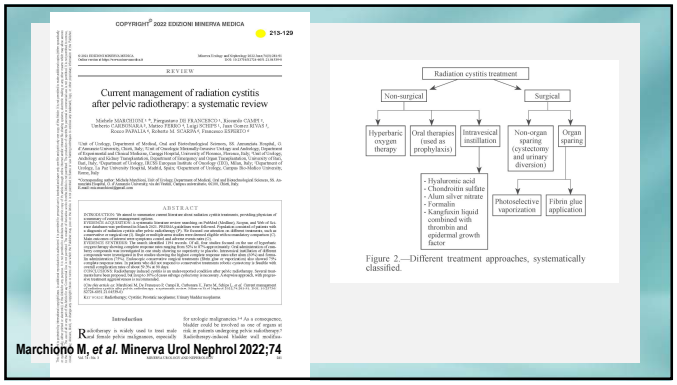
Radiation-induced cystitis treated with hyperbaric oxygen therapy (RICH-ART): a randomised, controlled, phase 2–3 trial

Oscarsson N, *et al.* Lancet Oncol 2019;20(11)



Development of a Management Algorithm for Acute and Chronic Radiation Urethritis and Cystitis

Vanneste B, *et al.* Urology Int. 2022;106:63-74



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213-129

REVIEW

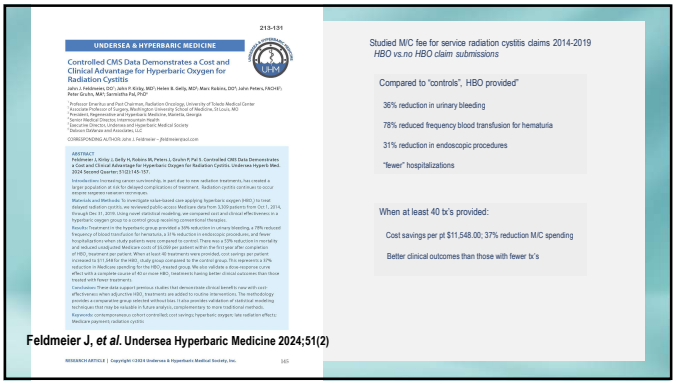
Current management of radiation cystitis after pelvic radiotherapy: a systematic review

Michele MARCHIONNI 1 *, Piergiuseppe DE FRANCESCO 1, Riccardo CIARPI 1, Umberto CARDINALE 1, Matteo FERRO 1, Luigi SCIETTI 1, Jean Gomez RIVAS 1, Rocco PAPALIA 1, Roberto M. SCARONI 2, Francesco ESPOSITO 1

ABSTRACT

Marchiono M. *et al.* Minerva Urol Nephrol 2022;74

Figure 2.—Different treatment approaches, systematically classified.



213-131

UNDERSEA & HYPERBARIC MEDICINE

Controlled CMS Data Demonstrates a Cost and Clinical Advantage for Hyperbaric Oxygen for Radiation Cystitis

ABSTRACT

Studied M/C fee for service radiation cystitis claims 2014-2019
HBO vs.no HBO claim submissions

Compared to "controls", HBO provided"

36% reduction in urinary bleeding

78% reduced frequency blood transfusion for hematuria

31% reduction in endoscopic procedures

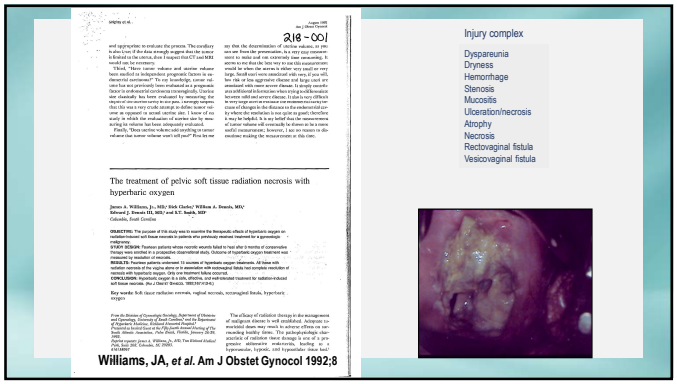
"fewer" hospitalizations

When at least 40 tx's provided:

Cost savings per pt $11,548.00; 37% reduction M/C spending

Better clinical outcomes than those with fewer tx's

Feldmeier J, *et al.* Undersea Hyperbaric Medicine 2024;51(2)



218 - 001

The treatment of pelvic soft tissue radiation necrosis with hyperbaric oxygen

James A. Williams, Jr., MD,* Rick Charles,† William A. Dennis, MD,‡ Edward J. Davis, III, MD,§ and K.C. Isaacs, MD*

Colombia, South Carolina

Injury complex

Dyspareunia
Dryness
Hemorrhage
Stenosis
Mucositis
Ulceration/necrosis
Atrophy
Necrosis
Rectovaginal fistula
Vesicovaginal fistula

Williams, JA, *et al.* Am J Obstet Gynocol 1992;8

218-024

PRACTICE GUIDELINE SERIES

Hyperbaric oxygen therapy for late radiation tissue injury in gynecologic malignancies

ABSTRACT

KEY WORDS

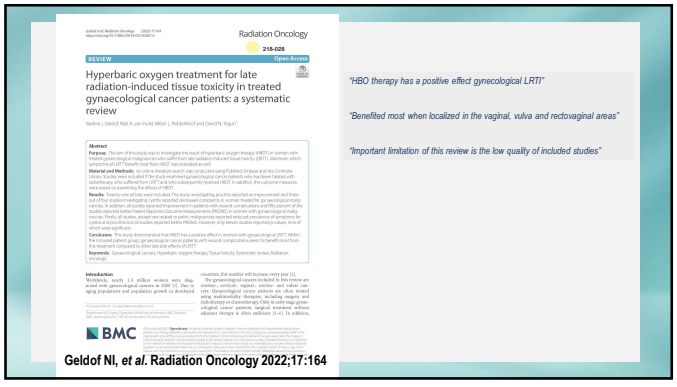
218-023

ORIGINAL ARTICLE

The use of hyperbaric oxygen for treating delayed radiation injuries in gynecologic malignancies: a review of literature and report of radiation injury incidence

Craighead P, *et al.* Current Oncology 2011;18(5)

Allen S, *et al.* Support Care Cancer 2012;20



Radiation Oncology

218-028

REVIEW

Open Access

Hyperbaric oxygen treatment for late radiation-induced tissue toxicity in treated gynaecological cancer patients: a systematic review

Nadine I. Geldof, Reid A. von Hulst, Milan L. Rikkerink and David N. Yeung*

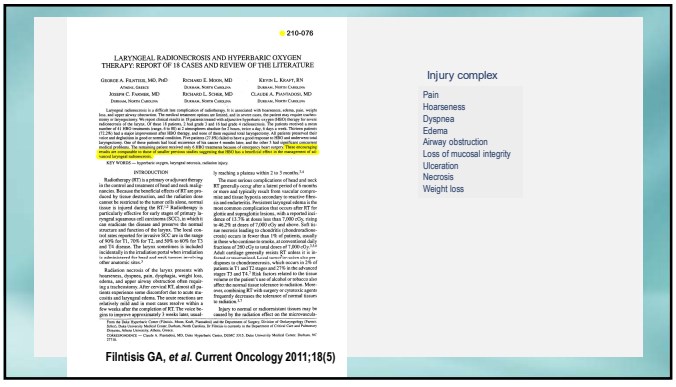
Abstract

Geldof NI, *et al.* Radiation Oncology 2022;17:164

"HBO therapy has a positive effect gynecological LRTI"

"Benefited most when localized in the vaginal, vulva and rectovaginal areas"

"Important limitation of this review is the low quality of included studies"



210-076

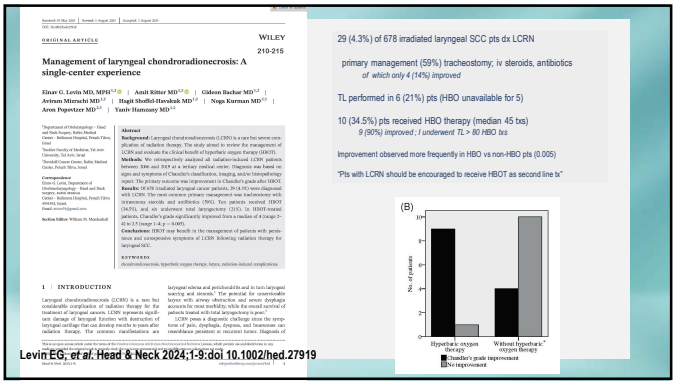
LARYNGEAL RADIONECROSIS AND HYPERBARIC OXYGEN THERAPY: REPORT OF 18 CASES AND REVIEW OF THE LITERATURE

Injury complex

Pain
Hoarseness
Dysphea
Edema
Airway obstruction
Loss of mucosal integrity
Ulceration
Necrosis
Weight loss

Filntisis GA, *et al.* Current Oncology 2011;18(5)

Abe M, *et al.* Jpn J Radiol 2012;30(4)



Levin EG, *et al.* Head & Neck 2024;1-9:doi 10.1002/hed.27919

Hyperbaric dosing

Treatment pressure…2.0 ATA oxygen

may require a multiplace (mask) pressure of 2.36 ATA

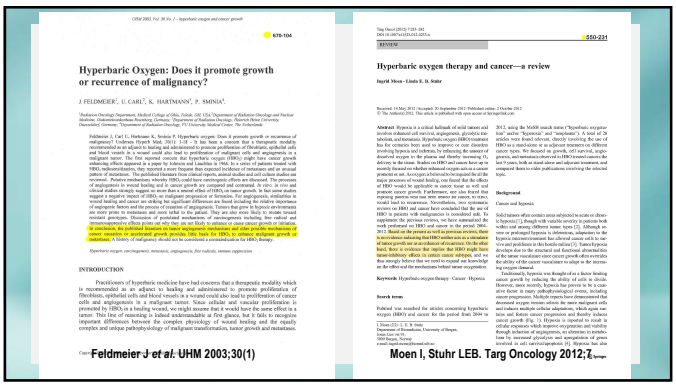
Treatment duration…90 minutes at tx pressure

typically requires up to 120 minutes in-chamber time

Treatment frequency…once daily, five times weekly

Treatment course…30-40 exposures

titrated to clinical response



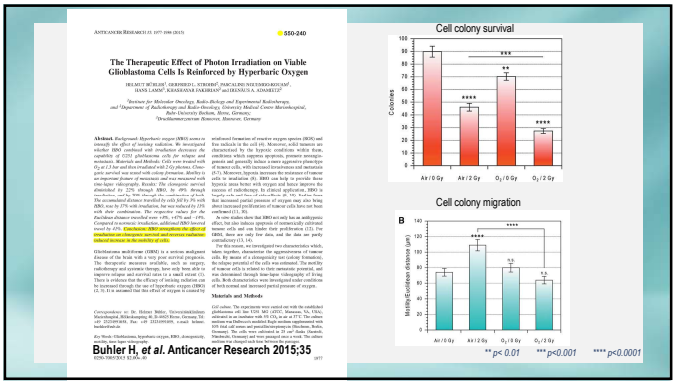
Feldmeier J *et al.* UHM 2003;30(1)

Moen I, Stuhr LEB. Targ Oncology 2012;7

Five-Year Recurrence Rates for SCC

SCC Stage	Non-HBO	Recurred	HBO	Recurred
I	29	6 (21%)	36	6 (16%)
II	58	14 (24%)	94	17 (18%)
III	50	16 (32%)	92	19 (21%)
IV	23	9 (38%)	23	6 (28%)

Marx RE, 2008
Hyperbaric Med Practice



ANTICANCER RESEARCH 35: 1977-1984 (2015)

S50-240

The Therapeutic Effect of Photon Irradiation on Viable Glioblastoma Cells Is Reinforced by Hyperbaric Oxygen

HELMUT BUHLER[1], GEORGES L. STRAMBI[1], PASCALINE NOUVEAU-KNAUP[1], HANS LAMM[1], KHASHAYAR FAKHRIAN[2] and HERMES D. A. EMAMI[1,2]

[1]*Institute for Molecular Oncology, Radiobiology and Experimental Radiotherapy, and* [2]*Department of Radiotherapy and Radio-Oncology, University Medical Centre Mannheim(a), Ruhr-University Bochum, Herne, Germany;* [3]*Oncoblastomyces.com Homecare, Moncton, Germany*

Abstract. *Background: Hyperbaric oxygen (HBO) seems to intensify the effect of ionising radiation. We investigated whether HBO combined with irradiation decreases the capability of U251 glioblastoma cells for relapse and metastasis. Materials and Methods: Cells were irradiated with 0, 2 or 12 Gy and then irradiated with 2 Gy photons. Clonogenic survival was tested with colony formation. Motility is an important feature of metastasis and was measured with time-lapse videography. Results: The clonogenic survival fraction after 2 Gy was reduced by 50% under HBO, as compared to normoxic irradiation. The accumulated distance travelled by cells fell by 3% with HBO, was by 17% with irradiation, but was reduced by 33% with their combination. The respective values for the Euclidean distance were 4%, 20% and 40%. Conclusion: HBO boosted by 43%. Conclusion: HBO strengthens the effect of irradiation on clonogenic survival and reverses radiation-induced increase in the motility of cells.*

Glioblastoma multiforme (GBM) is a serious malignant disease of the brain with a very poor survival prognosis. The therapeutic measures available, such as surgery, radiotherapy and systemic therapy, have only been able to achieve a moderate increase in survival in the past years. There is evidence that the efficacy of ionising radiation can be increased through the use of hyperbaric oxygen (HBO) (1, 2). It is assumed that this effect of oxygen is caused by

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Key Words: Glioblastoma, hyperbaric oxygen, HBO, clonogenicity, motility, time-lapse videography.

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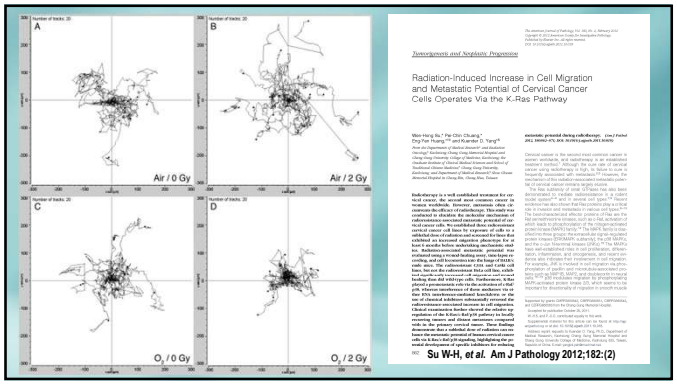
ISSN 1791-7530 E-ISSN 1791-7549

Buhler H, *et al.* Anticancer Research 2015;35

** p< 0.01 *** p<0.001 **** p<0.0001



Tumorigenesis and Neoplastic Progression

Radiation-Induced Increase in Cell Migration and Metastatic Potential of Cervical Cancer Cells Operates Via the K-Ras Pathway

Wen-Hong Su,* Pei-Chin Chuang,* Ding-Fan Huang,[†‡] and Kuan-Der D. Yang[§¶]

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Radiotherapy is a well established treatment for cervical cancer, the second most common cancer in women worldwide. However, metastasis often circumvents the efficacy of radiotherapy. This study was conducted to elucidate the molecular mechanisms of radiation-induced metastasis in human cervical cancer cells. We established three radioresistant cervical cancer cell lines by exposure of cells to a fractionated dose of ionizing radiation. These cells exhibited an increased migratory phenotype for at least 6 weeks before undertaking cytochemistry studies. Radiation-induced migration was also investigated using a wound-healing assay, time-lapse recording, and cell locomotion into the lungs of SCID/Beige mice. Irradiation increased the motility of HeLa cells, but not the radioresistant HeLa cell line, which had significantly increased cell migration and wound healing. Activation of the K-Ras pathway was implicated as a prominent role via the activation of Akt/mTOR, whereas interference of these molecules via either DNA interference-mediated knockdown or the use of chemical inhibitors substantially reversed the radiation-induced migration of cervical cancer cells. Clinical examinations further showed the relative up-regulation of the K-Ras/Raf/p38 pathway in locally recurrent cervical cancer tissues after radiotherapy, with or the primary cervical cancer. These findings demonstrate that a sublethal dose of radiation can enhance the migration potential of human cervical cancer cells via K-Ras/Akt/p38 signaling, highlighting the potential development of specific inhibitors for enhancing

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W.-H.S. and P.-C.C. contributed equally to this work.

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Su W-H, *et al.* Am J Pathology 2012;182:(2)