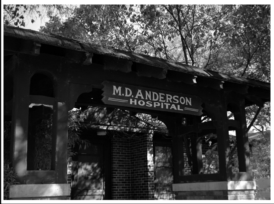
Transitioning from 3D IMRT to 4D IMRT and the Role of Image Guidance

Part II: Thoracic

Peter Balter, Ph.D.



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MD Anderson ~~Cancer~~ Center

Disclosure

Å Dr. Balter is Physics PI on a trial comparing Cyberknife based SBRT with surgery, funded by Accuray

Å Dr. Balter is co-PI on a sponsored research agreement with Philips Medical Systems.

Å MDACC has a sponsored research agreement with Varian Medical Systems (Dr. Balter is not named on this agreement but Varian equipment is presented in this course)

Outline

Å IMRT in the Lung

Å Inter-fraction motion of thoracic tumors (4DCT)

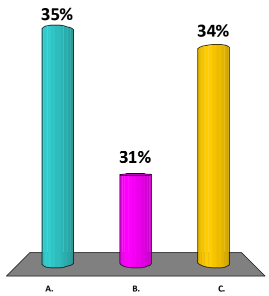
Å How to treat tumors that move with respiration

Å IMRT and tumor motion/Interplay effect

Å Thoracic tumor volumes changing with time (the other 4th D)

Are you using IMRT in the lung

A. No
B. Yes for all cases
C. Yes for selective cases



How is IMRT in the lung different from other sites

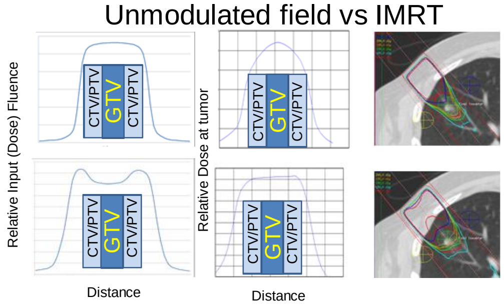
Å All sites
- ï Create a conformal dose distribution

Å Prostate
- ï Create concave dose distributions around avoidance structures

Å Head and Neck
- ï Multiple targets at different dose levels

Å Lung
- ï Compensate for different scatter conditions
  - ÅBetween the GTV and CTV (between tissue and air)
  - ÅBetween center and sides of targets
  - ÅBetween medial and lateral sides of targets
- ï And the other stuff from prostate and H&N

Example: Small Mass in Lung Unmodulated field vs IMRT



Am J Clin Oncol. 2003 Feb;26(1):70-8.

Reduction in radiation dose to lung and other normal tissues using helical tomotherapy to treat lung cancer, in comparison to conventional field arrangements.

Scrimger RA, Tomé WA, Olivera GH, Reckwerdt PJ, Mehta MP, Fowler JF.
Department of Human Oncology, University of Wisconsin, Madison, Wisconsin 53792, USA.

Å TomoTherapy study of 5 patients

Å Demonstrated

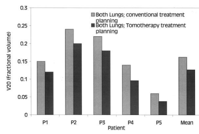
ï Improved tumor coverage

ï Reduced dose to all critical structures

TABLE 2. *Tumor doses delivered by conventional treatment planning and tomotherapy*

	EUD of gross tumor volume (Gy_{10})	
Patient	CFA	Tomotherapy
P1	63.4	65.0
P2	64.0	63.5
P3	63.5	66.3
P4	60.9	61.4
P5	62.9	64.2

CFA, conventional field arrangements; EUD, effective uniform dose.



Int J Radiat Oncol Biol Phys. 2004 Mar 15;58(4):1258-67.

Dose and volume reduction for normal lung using intensity-modulated radiotherapy for advanced-stage non-small-cell lung cancer.

Murshed H, Liu HH, Liao Z, Barker JL, Wang X, Tucker SL, Chandra A, Guerrero T, Stevens C, Chang JY, Jeter M, Cox JD, Komaki R, Mohan R.
Division of Radiation Oncology, University of Texas M. D. Anderson Cancer Center, Houston, TX 77030, USA.

Å 41 patients

Å Clinical 3D plans compared with IMRT plans

Å IMRT was more conformal

Å IMRT provided better sparing of critical structures

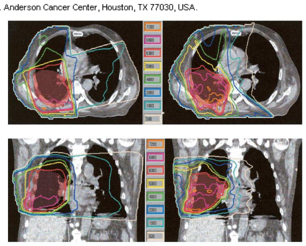


Fig. 1. Comparison of isodose distribution with (Left) 3D-CRT and (Right) IMRT in a single case. (a) Axial view. (b) Coronal view.

Int J Radiat Oncol Biol Phys. 2004 Mar 15;58(4):1258-67.

Dose and volume reduction for normal lung using intensity-modulated radiotherapy for advanced-stage non-small-cell lung cancer.

Murshed H, Liu HH, Liao Z, Barker JL, Wang X, Tucker SL, Chandra A, Guerrero T, Stevens C, Chang JY, Jeter M, Cox JD, Komaki R, Mohan R.
Division of Radiation Oncology, University of Texas M. D. Anderson Cancer Center, Houston, TX 77030, USA.

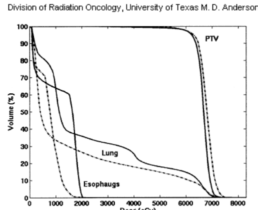


Table 3. Summary of the total lung V_5, V_{10}, and V_{20}, V_{eff}, mean dose, and integral dose for 3D-CRT and IMRT plans

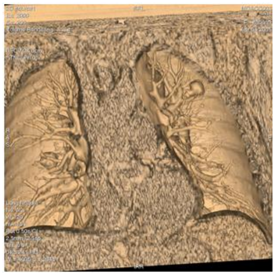
Parameter	3D-CRT	IMRT	p
Total lung V_5 (%)	52 (28–86)	59 (25–78)	0.424
Total lung V_{10} (%)	45 (22–64)	38 (18–59)	<0.0001
Total lung V_{20} (%)	35 ((17–55)	25 (13–43)	<0.0001
Total lung V_{eff} (%)	71 (33–101)	58 (28–95)	<0.0001
Total lung mean dose (Gy)	19 (10–29)	17 (9–27)	<0.0001
Total lung integral dose (J)	19 (5–36)	16 (5–34)	<0.0001

IMRT was shown to decrease lung at all levels except V_5

Why you should not use IMRT in Lung

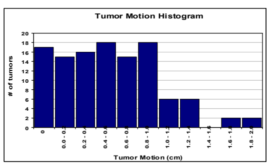
Å Interplay effect
- ï Step and shoot
- ï Sliding Window
- ï VMAT (Rapid Arc)

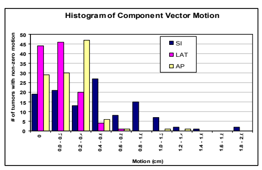
Å Geometric Miss
- ï Tumor motion
- ï Setup uncertainty



Both of these concerns are manageable !

How much do thoracic tumors move ?

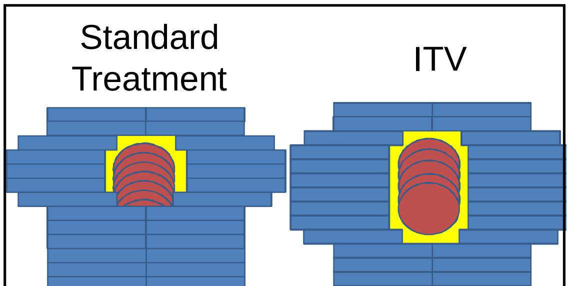




90% of thoracic tumors move less than 1 cm
50% move less than 5 mm

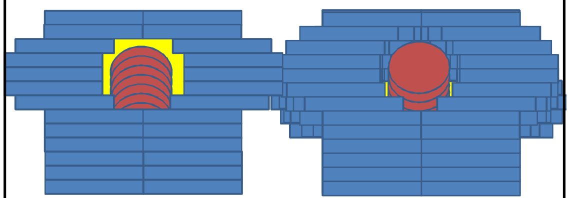
Assessing respiration-induced tumor motion and internal target volume using four-dimensional computed tomography for radiotherapy of lung cancer.

Liu HH, Balter P, Tutt T, Choi B, Zhang J, Wang C, Chi M, Luo D, Pan T, Hunjan S, Starkschall G, Rosen I, Prado K, Liao Z, Chang J, Komaki R, Cox JD, Mohan R, Dong L.



ITV : Treat track of tumor motion
Å Based on a 4-D dataset:
Å Explicitly account for tumor motion in delineating ITV
Å Optimize the plan based on respiratory motion

Gating / Tumor Tracking



Gating

Dynamic: Deliver dose when tumor is within the beam portal

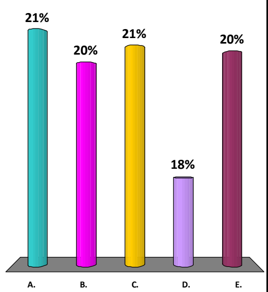
Breath-hold: Deliver the beam when breath is held at a given level

Tumor tracking

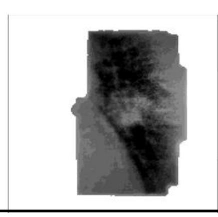
Follow the tumor with the beam portal

How is tumor motion accounted for at your clinic

A. Generic Margins
B. Patient specific margins determined from dynamic imaging (ie 4DCT)
C. Gating
D. B or C depending on the patient
E. A, B or C depending on the patient



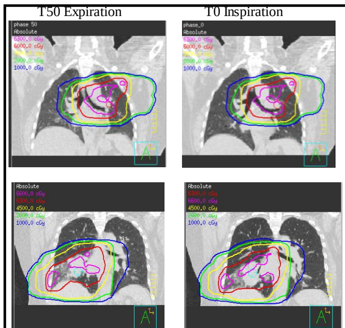
How does respiration affect dose distributions



Changes in Dose Distribution and DVH vs Respiration

- Å Megavoltage photons are relatively insensitive to local density changes
- Å Large doses differences occur only when objects move in and out of the dose distribution
- Å Changes in lung DVH are mainly due to changes in lung volume with respiration
- Å Changes in other DVHs only occur when object move in and out of the high dose region

T50 Expiration T0 Inspiration

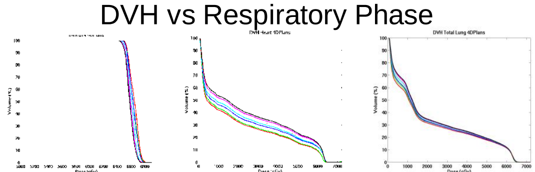


Away from diaphragm dose is stable/lung volume changes

Near diaphragm high dose region moves with diaphragm

ÅDose distribution remains relative stable during breathing except were it crosses the diaphragm
ÅHowever, lung volume is increased from expiration to inspiration

DVH vs Respiratory Phase



GTV Heart Lung

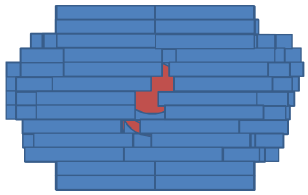
The DVH is a function of respiratory phase, but is generally bounded by the Inspiration and Expiration DVH

The choice of dataset for calculation is less important than using all the data for targeting (but donð use the MIP for heterogeneity corrections)

MDACC policy:

Determine the ITV from all datasets (MIP is a useful starting point)
Transfer the location of the target onto the calculation dataset (average or FB)
- by CT coordinates if all CTs are from the same imaging session
- by registering on anatomy that does not move with respiration

IMRT and the Interplay Effect



Some Publications on Interplay 1998-

Phys Med Biol. 1998 Jan;43(1):91-104.

The effects of intra-fraction organ motion on the delivery of dynamic intensity modulation.

Yu CX, Jaffray DA, Wong JW.

William Beaumont Hospital, Royal Oak, Michigan, USA.

Effects of intra-fraction motion on IMRT dose delivery: statistical analysis and simulation

Thomas Bortfeld *et al* 2002 *Phys. Med. Biol.* **47** 2203-2220

Radiother Oncol. 2001 Jul;60(1):95-105.

The effect of breathing and set-up errors on the cumulative dose to a lung tumor.

Engelsman M, Damen EM, De Jaeger K, van Ingen KM, Mijnheer BJ.

Department of Radiotherapy, The Netherlands Cancer Institute, Antoni van Leeuwenhoek Hospital, Plesmanlaan 121, 1066 CX Amsterdam, The Netherlands.

Med Phys. 2003 Jul;30(7):1736-46.

The effects of intra-fraction organ motion on the delivery of intensity-modulated field with a multileaf collimator.

Chui CS, Yorke E, Hong L.

Department of Medical Physics, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, New York 10021, USA. chuic@mskcc.org

Med Phys. 2006 May;33(5):1380-7.

Dosimetric and radiobiological impact of dose fractionation on respiratory motion induced IMRT delivery errors: a volumetric dose measurement study.

Duan J, Shen S, Fiveash JB, Popple RA, Brezovich IA.

Department of Radiation Oncology, University of Alabama at Birmingham, Birmingham, Alabama 35233, USA. jduan@uabmc.edu

Med Phys. 2007 Mar;34(3):923-34.

Effects of organ motion on IMRT treatments with segments of few monitor units.

Seco J, Sharp GC, Turcotte J, Gierga D, Bortfeld T, Paganetti H.

Department of Radiation Oncology, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts 02114, USA.

Med. Phys. **37**, 5850 (2010); http://dx.doi.org/10.1118/1.3496356 (*8 pages*)

Use of a realistic breathing lung phantom to evaluate dose delivery errors

Laurence E. Court, *Dana-Farber Cancer Institute and Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts 02115*; Joao Seco, *Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts 02114*; Xing-Qi Lu, *Beth-Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts 02130*; Kazuyu Ebe, *JA Jouetsu Hospital, Jouetsu 355-0063, Japan*; Charles Mayo, *University of Massachusetts Memorial Medical Center, Worcester, Massachusetts 01655*; Dan Ionascu, *William Beaumont Hospital, Royal Oak, Michigan 48073*; Brian Winey, *Dana-Farber Cancer Institute and Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts 02115 and Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts 02114*; Nikos Giakoumakis, Michalis Aristophanous, Ross Berbeco, Joerg Rottman, Madeleine Bogdanov, Deborah Schofield, and Tania Lingos, *Dana-Farber Cancer Institute and Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts 02115*

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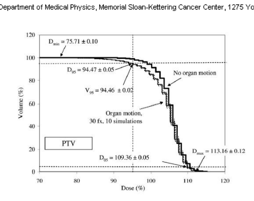


FIG. 11. Dose volume histograms for the PTV of lung patient #1. The solid and the dotted lines show the DVH without and with organ motion, respectively. Each dotted line represents one simulation of 30 fractions. There are a total of 10 simulations. The statistics show the mean and standard deviation of the 10 simulations with organ motion. The amplitude of the organ motion was $A = \pm 10$ mm. There is degradation of PTV coverage due to organ motion.

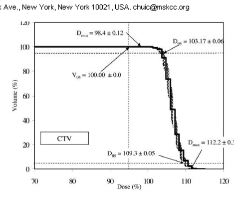


FIG. 12. Dose volume histograms for the CTV of lung patient #1. The solid and the dotted lines show the DVH without and with organ motion, respectively. Each dotted line represents one simulation of 30 fractions. There are a total of 10 simulations. The statistics show the mean and standard deviation of the 10 simulations with organ motion. The amplitude of the organ motion was $A = \pm 10$ mm. The coverage of CTV was not much affected by the organ motion, implying a sufficient PTV margin.

PTV coverage is compromised by not CTV

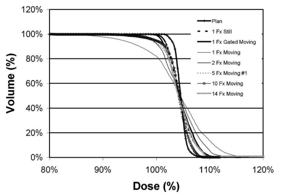
- PTV did itôs job (assuming a portion of PTV was internal margin (IM).

Med Phys. 2006 May;33(5):1380-7.

Dosimetric and radiobiological impact of dose fractionation on respiratory motion induced IMRT delivery errors: a volumetric dose measurement study.

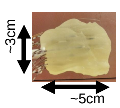
Duan J, Shen S, Fiveash JB, Popple RA, Brezovich IA.
Department of Radiation Oncology, University of Alabama at Birmingham, Birmingham, Alabama 35233, USA. jduan@uabmc.edu

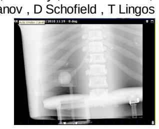
- Phantom measurements of sliding window IMRT
- Included Radiobiological effect modeling
- Showed stability at 5 fractions with no effect on TCP



Treatment of Moving Tumors: An Inter-Modality Comparison Under Realistic Clinical Conditions

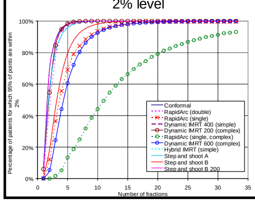
L Court , J Seco , X Lu , K Ebe , C Mayo , D Ionascu , B Winey , N Giakoumakis, M Aristophanous , R Berbeco , J Rottmann , M Bogdanov , D Schofield , T Lingos



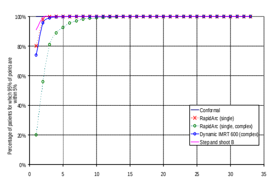


Effect of fractionation

2% level



5% level



Common conclusions

- Interplay effects can be large for small number of fractions
- Interplay effects cancel out over a large number of fractions
- Interplay effect can be minimized
  - Choosing MLC direction
  - Lowering modulation
  - Lowering dose rate
  - Gating
- Appropriate margins are more important than interplay effect

IGRT, Margins and Localization in the Thorax

IGRT in the thorax

Å Reduced margins (or achieve the ones we have been planning with)
Å Gating with verification
Å Adaptive planning
  ï Correct for geometric miss
  ï Adapt to changing anatomy

How well are we targeting in the thorax?

Int J Radiat Oncol Biol Phys. 2000 Jul 1;47(4):1121-35.

The probability of correct target dosage: dose-population histograms for deriving treatment margins in radiotherapy.

van Herk M, Remeijer P, Rasch C, Lebesque JV.

Radiotherapy Department, The Netherlands Cancer Institute/Antoni van Leeuwenhoek Huis, Amsterdam, The Netherlands. portal@nki.nl

Int J Radiat Oncol Biol Phys. 2009 Jul 15;74(4):1100-7. Epub 2009 Apr 22.

Tumor localization using cone-beam CT reduces setup margins in conventionally fractionated radiotherapy for lung tumors.

Yeung AR, Li JG, Shi W, Newlin HE, Chvetsov A, Liu C, Palta JR, Olivier K.

Department of Radiation Oncology, University of Florida College of Medicine, Gainesville, FL, USA.

Int J Radiat Oncol Biol Phys. 2009 Mar 1;73(3):927-34. Epub 2008 Dec 25.

Cone-beam computed tomographic image guidance for lung cancer radiation therapy.

Bissonnette JP, Purdie TG, Higgins JA, Li W, Bezjak A.

Radiation Medicine Program, Princess Margaret Hospital, Toronto, ON, Canada. jean-pierre.bissonnette@rmp.uhn.on.ca

Conclusions

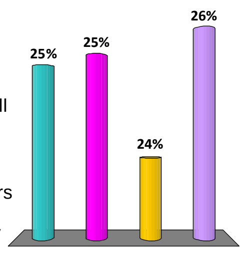
ÅBoney anatomy based setup reduced systematic errors
ÅNon-isotropic margins
ÅIGRT still requires appropriate PTV

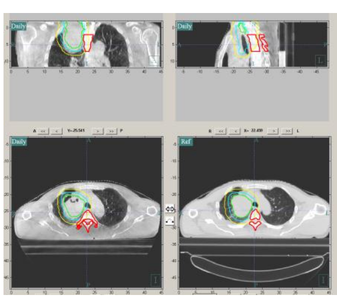
Adaptive Planning-Thorax

Å Many tumors change size and shape during the course of radiotherapy
Å Normal anatomy/breathing pattern can change more
Å If we do not adapt to these changes
  ï We may miss tumor
  ï We may overdose normal anatomy
  ï We may miss an opportunity to dose escalate
Å Thorax ï big cavity where tumor, fluid and air can all change places with no external indication
  ï Often the goal of radiotherapy is to open airways which then cause changes in internal anatomy

Do you regularly adapt for tumor changes in the thorax

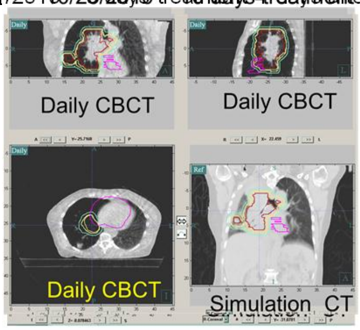
A. No
B. Yes based on scheduled re-simulation (ie resim at 4 weeks) but only for Small Cell
C. Yes based on scheduled re-simulation (ie resim at 4 weeks) for all thoracic cancers
D. Yes based on daily or weekly imaging





Week 2

10/11/2010 10/18/2010 – 5 days treatment 10/26/2010 … days after sim

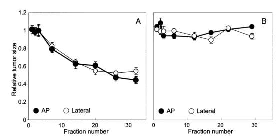


Radiother Oncol. 2003 Jan;66(1):75-85.

Portal imaging to assess set-up errors, tumor motion and tumor shrinkage during conformal radiotherapy of non-small cell lung cancer.

Erridge SC, Seppenwoolde Y, Muller SH, van Herk M, De Jaeger K, Belderbos JS, Boersma LJ, Lebesque JV.

Edinburgh Cancer Centre, Western General Hospital, Crewe Road South, Edinburgh, UK.



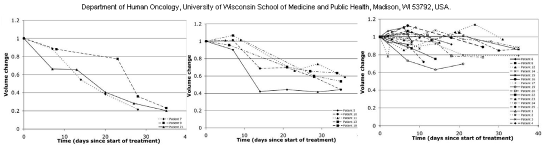
- Average reduction of 17%
- 10/25 regressed by > 20%
  - It took 4.5 ± 1(1 σ) week for this to occur

Int J Radiat Oncol Biol Phys. 2006 Sep 1;66(1):135-41. Epub 2006 Jul 12.

Tumor volume changes on serial imaging with megavoltage CT for non-small-cell lung cancer during intensity-modulated radiotherapy: how reliable, consistent, and meaningful is the effect?

Siker ML, Tomé WA, Mehta MP.

Department of Human Oncology, University of Wisconsin School of Medicine and Public Health, Madison, WI 53792, USA.

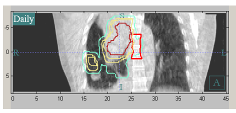


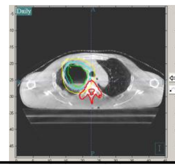
- Patients were put in three groups Partial Response, Marginal Response, or Stable Disease
- "No patient treatment, or tumor characteristics were found to be associated with tumor regression"
- It is not know if the CTV shirks at the same rate as the GTV

When to adapt the plan

Å When the anatomy shifts
- ï Plan should be changed
- ï Isocenter should be moved
- ï New reference images need to be establish

Å When the tumor (GTV) shrinks
- ï Does the CTV shrink as well





3DIMRT to 4DIMRT ï Summary of Part 2

Å IMRT allows dose distributions high conformal to the treatment volume

Å IMRT requires appropriate margins
- ï Motion
- ï Setup
- ï Changes in anatomy

Å If IMRT is adapted without taking these factors into effect it may decrease local control

Å Dose escalation possible with IMRT is greater than the dose uncertainty related to interplay

Å 4DCT, IMRT, and IGRT have the potential to allow us to create dose distributions highly conformal to the suspected area of disease and with higher dose
- ï Without decreasing TCP due to geometric missed
- ï Without increasing NTCP due to large margins

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Å Chris Nelson, Ph.D.
Å Julianne Pollard, Ph.D.
Å Joe Chang, M.D., Ph.D.
Å James Cox, M.D.
Å Thomas Guerrero, M.D., Ph.D.
Å Ritsuko Komaki, M.D.
Å Xiandong Liao, M.D.
Å Steven Lin, M.D., Ph.D.
Å Craig Stevens, M.D., Ph.D.

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