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Authors: Thames, H. D., Hunter, N. R., and Mason, K. A.

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The Withers Archive: Online Availability of H. Rodney Withers' Data

H. D. Thames, a,1 N. R. Hunter and K. A. Mason

Departments of a Biostatistics and b Experimental Radiation Oncology, MD Anderson Cancer Center, Houston, Texas

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Dr. H. Rodney Withers (1932–2015) (1, 2) was one of the preeminent radiation biologists of his time, beginning in the 1960s and spanning more than 4 decades. He was a translational researcher who recognized the importance of stem cells and who asked questions about biological systems relevant to clinical practice. Dr. Withers was the embodiment of a translational physician scientist well before the concept became popular. His preclinical mouse data provided clinical radiation therapists rational guidelines for making treatment choices easily understood and highly accessible. "The 4 R's of Radiotherapy" coined by him summarized the key mechanisms governing tumor and normal tissue responses to fractionated radiotherapy while providing the biological bases to alter dose fractionation schemes for clinical benefit. In many ways, providing the data based rationale for exploiting these responses sums up his legacy for the radiation sciences. Repair of sublethal damage preferentially spares late responding normal tissues. Reassortment of surviving cells within the division cycle resensitizes rapidly proliferating cells. Reoxygenation of hypoxic cells during fractionated treatment radiosensitizes tumors. Repopulation of surviving clonogenic cells during a course of treatment is a hazard best minimized in the case of tumors and encouraged for acute responding normal tissues.

Prior to his death from Parkinson's disease in 2015, his long-time colleagues Kathy Mason and Howard Thames discussed with him about making his immense data base of normal tissue responses available to the worldwide scientific community by converting his handwritten lab notebooks into searchable digitized data files. Dr. Withers wholeheartedly agreed and over a span of 4 years, tens of thousands of animal observations were digitized by Nancy Hunter into the "Withers Archive". Some of these results have never been analyzed or published, and as we and former collaborators enter retirement it would have been

impossible for future investigators to gain access to his data. For this reason, we have digitized the contents of the lab notebooks. It was Rod's hope and ours that this data will have interest to newer scientists in the fields of radiation oncology and biology and their future use of this data base will continue to benefit cancer patients now and in the future. In this note we wish to explain the mechanism we have set up to make the raw data contained in the "Withers Archive" available to researchers online.

Organization of the Data

The data have been stored in 23 Microsoft Excel files whose contents are briefly described in Table 1. The files are grouped either by tissue (e.g., jejunum) or the nature of the end point (e.g., acute skin reaction). The experimental design is briefly described. Relevant publications (when available) are cited for each file.

Each of the 23 Excel files contains two sheets. The first sheet, titled "Explanatory", sets out the details of the experiments, including radiation source, strain of mice, fractionation schedule, etc. In addition, the details of the data formatting are explained. The second sheet, titled "Data", contains the digitized data.

A researcher who is interested in obtaining portions of this data would begin by identifying what parts are wanted, according to the terminology used in Table 1. Afterward, please ensure that this terminology is used when contacting staff at the Center for Radiation Oncology Research (CROR) at MD Anderson Cancer Center (as explained in more detail below).

Two-Step Exchange of Emails to Obtain the Data

First step. The requestor identifies the tissues/end points of interest from Table 1. The requestor then sends an email to the staff at CROR (CRORadmin@mdanderson.org) requesting more detailed information. The staff at CROR will then match the requested tissues/end points (using the terminology from Table 1) to various "synopses", which set out the contents of the Excel files in detail. The appropriate synopses will be emailed to the requestor.

Second step. The requestor uses the synopses to identify specific Excel files that match their needs, and emails that

TABLE 1

		Excel	
Data (no. obs.)	Assay	file no.	Experimental design (refs.)
Jejunum (7644)	Microcolony	File 1	Variable dose/fraction and interval (3,4)
		File 2	Variable dose rate (5, 6)
		File 3	Proton, ⁶⁰ Co, ¹³⁷ Ce single doses, neutron single and fractionated (7–10)
		File 4	Regeneration, variable overall time
		File 5	Recovery after 1st dose, variable dose/fraction interval
		File 6	Variable dose rate, dose/fraction and interval (11, 12)
		File 7	Variable dose/fraction and interval (9, 13)
		File 8	Variable dose/fraction and interval, X rays (14, 15)
Colon (5210)	Microcolony	File 9	Variable dose/fraction, interval (16, 17)
Testis (5192)	Microcolony	File 10	Variable dose/fraction, interval and dose rate, neutron (18–21)
Acute skin reaction (4867)	Reaction score	File 11	Variable dose/fraction and interval (22, 23)
		File 12	Variable dose/fraction, interval and dose rate
		File 13	Repopulation (24)
		File 14	Strain comparison (C3H vs. C57), repopulation
Leg and skin contraction (3724)	Skin and leg contraction	File 15	Variable dose/fraction and interval (22, 25, 26)
		File 16	Variable dose/fraction and interval
		File 17	Strain comparison (C3H vs. C57), Repopulation
Retreatment skin reaction (622)	Acute reaction score and skin contraction	File 18	Variable dose/fraction with and without pretreatment (27–29)
Bone (314)	Growth retardation	File 19	Variable dose/fraction (30)
Hair (1583)	Microcolony	File 20	Variable dose/fraction and dose rate for resting and proliferative states (31)
Kidney (1084)	Microcolony	File 21	Variable dose/fraction & interval (32)
Spinal cord (785) guinea pig	Paralysis	File 22	Variable dose/fraction, retreatment at 28 or 40 weeks (33, 34)
Bone marrow (211)	Endogenous spleen colony assay	File 23	Variable dose/fraction (35)

list of Excel files back to CRORadmin@mdanderson.org. The requested files are then emailed back to the requestor.

Acknowledgment of Re-publication

If the data provided as described in this note are used in any future publications, it is requested that the following acknowledgment be cited: "Data used in this study were obtained from the Withers Archive, the digitization of results from the research groups of H.R. Withers and his colleagues were provided by the Center for Radiation Oncology Research at the MD Anderson Cancer Center".

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REFERENCES

- McBride WH, Mason KA, Peters LJ, Thames HD. Dr. H. Rodney withers (1932 - 2015). Int J Radiat Biol 2015; 91:459–61.
- McBride WH, Mason KA, Peters LJ, Thames HD. In memoriam: H. Rodney Withers (21 September 1932 – 25 February 2015). Radiat Res 2015; 183:586–8.
- Thames HD Jr, Withers R, Mason KA, Reid BO. Dose-survival characteristics of mouse jejunal crypt cells. Int J Radiat Oncol Biol Phys 1981; 11:1591–7.
- Thames HD Jr, Withers HR. Test of equal effect per fraction and estimation of initial clonogen number in microcolony assays of survival after fractionated irradiation. Br J Radiol 1980; 53:1071– 7.

- Withers HR. Cell renewal system concepts and the radiation response. In: Frontiers of Radiation Therapy Oncology. Karger, Basel & University Park Press; 6:93–107, 1972.
- Mason KA, Thames HD, Ochran TG, Ruifrok AC, Janjan N. Comparison of continuous and pulsed low dose rate brachytherapy: biological equivalence in vivo. Int J Radiat Oncol Biol Phys 1994; 28:667–71.
- Mason KA, Gillin MT, Mohan R, Cox JD. Preclinical biologic assessment of proton beam relative biologic effectiveness at Proton Therapy Center Houston. Int J Radiat Oncol Biol Phys 2007; 68:968–70.
- 8. Withers HR, Mason K, Reid BO, Dubravsky N, Barkley HT Jr, Brown BW, Smathers JB. Response of mouse intestine to neutrons and gamma rays in relation to dose fractionation and division cycle. Cancer 1974; 34:39–47.
- Withers HR, Chu AM, Mason KA, Reid BO, Barkley HT Jr, Smathers JB. Response of jejunal mucosa to fractionated doses of neutrons or gamma-rays. Eur J Cancer 1974: 249–52.
- 10. Hall EJ, Withers HR, Geraci JP, Meyn RE, Rasey J, Todd P, Sheline GE. Radiobiological intercomparisons of fast neutron beams used for therapy in Japan and the United States. Int J Radiat Oncol Biol Phys 1979; 5:227–33.
- 11. Meyn RE, Peters LJ, Mills MD, Moyers MF, Fields RS, Withers HR, Mason KA. Radiobiological aspects of electron beams. The role of high energy electrons in the treatment of cancer. In: Frontiers of Radiation Therapy Oncology. Vol. 25. In: Vaeth JM, Meyer JL, editors. Karger: Basel, 1991: p. 53–60.
- Mason KA, Withers HR, McBride WH, Davis CA, Smathers JB. Comparison of the gastrointestional syndrome after total-body or total-abdominal irradiation. Radiat Res 1989; 117:480–8.
- 13. Withers HR, Reid Bo, Hussey DH. Response of mouse jejunum to

- multifraction radiation. Int J Radiat Oncol Biol Phys 1975; 1:41-52
- 14. Sheu T, Molkentine J, Transtrum MK, Buchholz TA, Withers HR, Thames HD, Mason KA. Use of the LQ model with large fraction sizes results in underestimation of isoeffect doses. Radiother Oncol 2013; 109:21–5.
- Wiedenmann N, Valdecanas D, Hunter N, Hyde S, Buchholz TA, Milas L, Mason KA. 130-nm albumin-bound paclitaxel enhances tumor radiocurability and therapeutic gain. Clin Cancer Res 2007; 13:1868–74.
- Tucker SL, Withers HR, Mason KA, Thames HD Jr. A dosesurviving fraction curve for mouse colonic mucosa. Eur J Cancer Clin Oncol 1983; 19:433–7.
- Withers HR, Mason KA. The kinetics of recovery in irradiated colonic mucosa of the mouse. Cancer 1974; 34:suppl:896-903.
- Withers HR, Hunter N, Barkley HT Jr, Reid BO. Radiation survival and regeneration characteristics of spermatogenic stem cells of mouse testis. Radiat Res 1974; 57:88–103.
- Suzuki N, Withers HR. Exponential decrease during aging and random lifetime of mouse spermatogonial stem cells. Science 1978; 202:1214–5.
- Meistrich ML, Hunter NR, Suzuki N, Trostle PK, Withers HR. Gradual regeneration of mouse testicular stem cells after exposure to ionizing radiation. Radiat Res 1978; 74:349–62.
- Thames HD Jr, Withers HR. Test of equal effect per fraction and estimation of initial clonogen number in microcolony assays of survival after fractionated irradiation. Br J Radiol 1980; 53:1071– 7.
- Masuda K, Hunter N, Stone HB, Withers HR. Leg contracture in mice after single and multifractionated 137Cs exposure. Int J Radiat Oncol Biol Phys 1987; 13:1209–15.
- Masuda K, Matsuura K, Withers HR, Hunter N. Age dependency of response of the mouse skin to single and multifractionated gamma irradiation. Radiother Oncol 1986; 7:147–53.
- Ruifrok AC, Mason KA, Hunter N, Thames HD. Changes in the radiation sensitivity of mouse skin during fractionated and prolonged treatments. Radiat Res 1994; 139:334–43.

- Masuda K, Hunter N, Withers HR. Late effect in mouse skin following single and multifractionated irradiation. Int J Radiat Oncol Biol Phys 1980; 6:1539

 –44.
- Masuda K, Hunter N, Withers HR. Early skin shrinkage in mice after single and multifractionated gamma-ray exposure. J Radiat Res 1982; 23:313–27.
- Masuda K, Matsuura K, Withers HR, Hunter N. Response of previously irradiated mouse skin to a second course of irradiation: early skin reaction and skin shrinkage. Int J Radiat Oncol Biol Phys 1986; 12:1645–51.
- Masuda K, Hunter N, Withers HR, Matsuura K. Radiosensitivity
 of irradiated mouse skin to a second course of single and
 multifractionated irradiation. I. Early skin reaction. Radiat Med
 1983: 1:85–8.
- Jingu K, Masuda K, Withers HR, Hunter N. Radiosensitivity of pre-irradiated mouse skin to second courses of single and multifractionated irradiation—skin shrinkage. Radiother Oncol 1989; 14:143-50.
- Masuda K, Reid BO, Hunter N, Withers HR. Bone growth retardation induced by single and multifractionated irradiation. Radiother Oncol 1990; 18:137–45.
- Tucker SL, Thames HD, Brown BW, Mason KA, Hunter NR, Withers HR. Direct analyses of in vivo colony survival after single and fractionated doses of radiation. Int J Radiat Biol 1991; 59:777– 95.
- Withers HR, Mason KA, Thames HD Jr. Late radiation response of kidney assayed by tubule-cell survival. Br J Radiol 1986; 59:587– 95.
- 33. Mason KA, Withers HR, Chiang CS. Late effects of radiation on the lumbar spine cord of guinea pigs: re-treatment tolerance. Int J Radiat Oncol Biol Phys 993; 26:643–8.
- 34. Taylor JM, Mason KA, Vegesna V, Withers HR. A non-parametric method of reconstructing single-dose survival curves from multifraction experiments. Int J Radiat Biol 1998; 74:583–93.
- 35. Kogelnik HD, Withers HR. Radiobiological considerations in multifraction irradiation. Radiol Clin (Basel) 1978; 47:362–9.