(M1) leading to additional telomere attrition and (2) short telomeres induce genetic instability."[1p2250] The genetic alterations leading to a bypass of M1 (senescence) are in CLL probably 11q− (ATM ↓) and 17p− (p53 ↓).[2] CLL cells with these aberrations in general have unmutated *IGHV* genes[3,4] and it can also be assumed that these cells from the start have shorter telomeres than B cells with mutated *IGHV* genes.[5,6] We also wrote "11q− or 17p− aberration in combination with overexpression of ZAP-70 and/or CD38 give cells a survival advantage and facilitate cell cycle progression, one consequence of which is telomere attrition."[1p2250] In addition, we referred to the report showing a correlation between birth rate and disease activity,[7] concluding that "[t]hese data suggest that cell kinetic characteristics can contribute to differences in telomere length."[1p2250]

In summary, we argue that short telomeres can be a consequence of certain genetic aberrations leading to increased cell proliferation, and thus agree with Jahrsdörfer and Weiner, but we also believe that it is likely that the cell of origin differs in telomere length depending on its *IGHV* gene status. Critically short telomeres can thereafter induce a state of genetic instability leading to further genetic alterations.

Regarding the question "Short telomeres in B-CLL: The chicken or the egg?" we argue that the answer rather is "both," which means that the short telomere phenotype is the result of many interacting factors as outlined in our paper. The "chicken" is the telomere length in the cell of origin, and the "egg" includes a number of possible events (11p−/17p−, ZAP70 ↑, CD38 ↑, and others) with effects on cell cycle progression and survival.

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To the editor:

Radiologic and nuclear events: the METREPOL severity of effect grading system

The US approach to optimizing medical preparedness to a mass nuclear irradiation disaster has been nicely outlined in Weinstock et al,[1] and we thought it might be of interest, and relevance, to present in more depth the European approach referred to in the article.

In March 2002, the European Group for Blood and Marrow Transplantation (EBMT) established a Nuclear Accident Committee (NAC) to determine whether the EBMT resource of more than 500 hospital*s* could be optimized as a network for providing help in the event of a radiation disaster.[2]

In 2005, an EBMT International Consensus Meeting defined a unified basis for the medical management of radiation accident victims.[3] The core of this consensus was the 2001 "METREPOL" (**Me**dical **Tre**atment **P**roto**col**s for Radiation Accident) clinical grading of irradiated victims, based on data from 800 victims in 70 previous accidents.[4] METREPOL uses assessment of hematologic (H), neurovascular (N), cutaneous (C), and gastrointestinal (G) damage early after exposure to predict outcome.[4,5] It incorporates simple clinical laboratory tests such as haematologic blood counts, and, particularly, identifies the likelihood of "irreversible" (H4), and "reversible" (H3, H2, and H1) damage to the bone marrow.[6,7] METREPOL links the 4 systems (H, N, C, G) together, to identify early after exposure the potential for developing multiorgan failure.[8]

The US approach for predicting outcome is different and uses biodosimetry (chromosome changes in blood lymphocytes) as the driving force for deciding the outcome of a patient. However, in an emergency involving, say, 30 000 patients with myeloid suppression, the use of chromosome analysis to estimate a dose would be impossible simply due to logistic reasons.[1] With the "METREPOL" approach, the combination of clinical parameters and simple blood count changes would be logistically feasible.

In addition, we feel METREPOL may be a more accurate predictor of outcome. In the group of irradiated patients illustrated in Figure 1, there is a uniform pattern seen in blood parameters after irradiation, with an initial granulocytosis, followed by a drop by day 7. This identifies a homogeneous group of patients with irreversible damage to their stem cell pool (H4) such that they will need SCT rescue if they are to have a chance of survival.[6] However, the calculated biodosimetry in these same patients showed heterogeneity, with a wide estimated dose range from 8 to 20 Gy.

For triage after a mass radiation event, we feel that prehospital triage should take place, based on symptoms and the location of the patient during radiation exposure, to prevent blockade of hospitals. A second triage occurs at the referred hospital after decontamination.

Lastly, in the Weinstock paper there is little about training or communications. EBMT training started in November 2007 in Munich. We also have a network of electronic communication*s* in place, a key to optimizing allocation of irradiated patients to specialized hospitals. This facilitates real-time data collection, which not only allows for the best care but also is a research resource for future incidents and for optimizing METREPOL.

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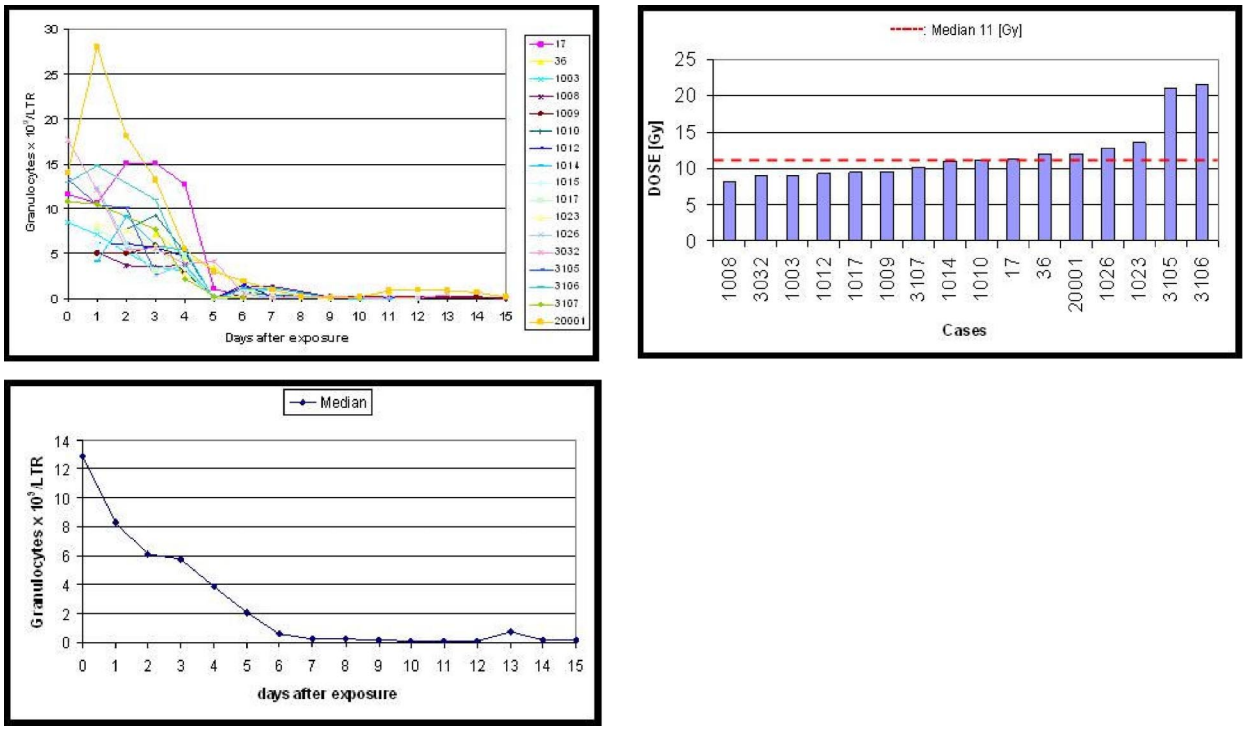

Figure 1. Granulocyte changes in 17 patients who are characteristic for a grading code H4 observed in 6 radiation accidents caused by whole body exposure to pure gamma or a mixed neutron/gamma radiation. An irreversible injury to the bone marrow stem cell pool can be assumed if the pattern of granulocyte concentration changes shows a severe granulocytopenia on days 5/6 (grade H4). However, the "dose" was reported to range from 8 to 20 Gy (median 11 Gy). A computerized program is under development to assess blood cell changes early after exposure and calculate the assignment of a patient to a grade H. The cases are documented in the database system SEARCH[5] and have been analyzed scientifically.[4,6,7,8] This figure was presented at the RITN meeting on September 25, 2007, in Bethesda, MD.

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Response

Radiologic and nuclear events

We thank Fliedner et al for their comments on our review[1] and look forward to collaborative efforts between the Radiation Injury Treatment Network (RITN) and the European Group for Blood and Marrow Transplantation (EBMT) to enhance event response, communication, and data collection. We agree that logistically cumbersome approaches to biodosimetry will not be useful for classifying the vast majority of victims after a mass casualty incident. Protocols that rely on clinical findings and/or peripheral blood cell counts, such as METREPOL (Medical Treatment Protocols for Radiation Accident Victims), are currently the most practical means for large-scale dosimetry.[2] In fact, the RITN Acute Radiation Syndrome Treatment Guidelines[3] incorporate the METROPOL assessment, but include additional dosimetry estimators that rely solely on time-to-vomiting or lymphocyte depletion kinetics.[4]

Although METREPOL can accurately identify victims of radiation accidents with irreversible marrow damage,[5] it does not clearly distinguish those who may benefit from hematopoietic stem cell transplantation from those who received invariably lethal doses. The latter group may best be served with only comfort measures. Also, METREPOL is based on collective experience from victims of radiation accidents. Important differences between accidental and intentional exposures may exist. For example, partial body shielding from buildings and other structures may